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BRITISH MEDICAL JOURNAL

LONDON SATURDAY FEBRUARY 7 1953

THE PRESENT STATUS OF LUNG RESECTION FOR PULMONARY TUBERCULOSIS

BY

F. H. YOUNG, M.D., F.R.C.P., D.P.H.

Physician to Brompton Hospital; Medical Officer in Charge of the Tuberculosis Dispensary, St. Bartholomew's Hospital; Consulting Physician, Charing Cross Hospital

In few conditions is there such a difference in the point of view of physicians and surgeons as in the treatment of pulmonary tuberculosis. For the part played by the surgeon is that of the character who comes into the play fairly late, monopolizes the most dramatic scene, and then takes little further active part in the play; whereas the physician is on the stage from the rise till the fall of the curtain.

As nearly all papers written on lung resection have emanated from surgeons, a physician's view may be useful. The material used consists of 26 cases of my own, and a further 52 made available to me by my colleagues at the Brompton Hospital: a total of 78. It includes practically every case in which resections were performed on *unhealed* tuberculous cases in 1949 and 1950 at Brompton Hospital, on the advice of physicians who had had resections performed on five or more cases; 80% of the cases have been followed up for a minimum of two years, and none for less than eighteen months. These years were selected as being those in which streptomycin was first freely available.

From the psychological point of view, resection of the diseased area of lung has a tremendous appeal to the patient and his doctor, as the immediate results are often dramatically good; hence there will be a great temptation to overdo the operation, and this will have to be guarded against till there is a more accurate assessment of its ultimate value than is at present possible. The patient tends to feel that, as the diseased tissue has been removed, he is no longer suffering from the disease or is infectious and will rapidly be able to resume a more or less normal life.

But this feeling of satisfaction and safety carries with it grave disadvantages. Examination of post-mortem material, and of the less diseased or apparently undiseased areas of lung which have had to be removed for technical reasons, and above all the appearance years later of areas of calcification in parts of lungs which have been previously radiologically normal, is illuminating. It proves that, in most cases, other parts of the lungs are usually the seat of much tuberculous disease. This implies that careful aftercare, with restriction on physical and general activity, must be carried out for a long time. It is difficult to persuade patients of the necessity for this, after a relatively short period of treatment culminating in what they are inclined to regard as a radical cure. Failure is particularly apt to occur when collaboration between physician and surgeon is not close. Surgical follow-up is a poor substitute for thorough aftercare.

It seems to me that the fundamental principle that the patient's fate depends on his resistance may be lost sight of. I feel that the suggestion—I acknowledge it is not more—put forward by the Liverpool School that pulmonary tuberculosis often is clinically a localized disease is full of danger.

Because we have removed the part of the lung which is an immediate bronchogenic menace and a source of toxaemia, it does not mean that other foci of disease, manifest or occult, will not progress in the near or distant future. For why did the patient get the diseased area which has been removed? Often it was not by bronchogenic spread from a manifest cavity or, in many cases to say the least of it, from an exogenous superinfection. On the other hand, resection has won for itself such a definite place in treatment that its use must be envisaged from the start and every effort made to avoid the production of streptomycin-resistant organisms. Evidence is accumulating that the risks of resection in streptomycin-resistant cases are many times greater than in sensitive cases.

Role of the Bronchus

It has been realized in the past few years that narrowing of the bronchi leading to cavities is one of the main reasons for the failure of collapse therapy to produce cavity closure; and, even if closure is obtained, residual tuberculous bronchiectasis may follow.

Speaking generally, resection is a better method of dealing with a lung in which bronchial stenosis is a prominent feature than is collapse therapy. Unfortunately, bronchoscopy is a very fallacious guide. The information derived from the average bronchoscopy is limited to a view of the condition of the openings of the main bronchi, and very often the obstruction is beyond. Some figures (Table I) which I obtained from Brompton Hospital cases illustrate this point.

TABLE I.—*Incidence of Bronchial Stenosis*

Total no. of resections		78
No. available for review		76
No stenosis found pathologically	26	
Stenosis found pathologically	50	
Stenosis found on bronchoscopy	31	

I have taken the reports of the bronchoscopies done immediately before resection operations, and the reports on the resected material. A caveat must be entered here. Unless the possibility is remembered, the bronchial obstruction in the resected lung may appear to be greater than it is in life. The proportion of cases with stenosis (66%) is very high, and in all probability even this figure is lower than the actual rate, because in some cases particular attention was not paid to this question, or at any rate its complete absence was not noted in the pathological report. The proportion of cases in which bronchoscopic evidence of stenosis is found is much smaller (40%). If, as I believe, the real place of resection is in the treatment of cases with bronchial stenosis, it is important that the pre-operative diagnosis of this should be made in as high a proportion as possible of the cases in which it occurs.

Is there any method by which the probability of stenosis can be suspected in the absence of bronchoscopic proof? A trial pneumothorax will often give a clue. After the first few insufflations with air it may be noted that an area corresponding to a lobe or major segment will be much more dense or contracted than the remainder of the lung. This may be taken to indicate that bronchial obstruction is probably present. If this occurs in the middle, lingula, or lower lobes the case should immediately be considered as a candidate for lung resection and the pneumothorax only kept up if it is thought that the patient can be got into better shape for resection, or if the surgeon prefers to carry out the resection with the pneumothorax in being.

In many bronchoscopic reports in which the absence of visible bronchial stenosis is alleged there appears the remark, "Secretion is seen coming from . . . "; and here follows the lobe bronchus, which subsequently is proved to be stenosed. Are we paying too little attention to minor bronchoscopic findings, which really indicate the high probability of occult bronchial stenosis?

The employment of lipiodol would be of great value, but among many workers there is still a feeling that the claim that aspiration spreads do not occur after its use is not quite true, and certainly residual lipiodol may be a nuisance. The use of the thick sulphathiazole-lipiodol mixture may prove to be the answer. Since using this I have had no evidence of any spread of disease and little residual lipiodol.

Artificial Pneumothoraces and Lung Resections

Of recent years most of those workers who have had extensive experience with artificial pneumothorax have felt that bronchial stenosis, obvious to bronchoscopy, is a contraindication to maintaining a pneumothorax, and even to its induction unless lung resection in the immediate future can be contemplated with equanimity. The figures which I have quoted indicate that occult bronchial stenosis is common, hence the possibility of its existence should be envisaged before inducing an artificial pneumothorax (A.P.). It has of late become the practice of many physicians to use streptomycin as a preparatory method of treatment before the induction of pneumothorax in acute and toxic cases. The use of P.A.S. in conjunction with it has reduced the likelihood of producing streptomycin-resistant organisms. Where, however, there is a chronic cavity, either in the lung under consideration or on the other side, the likelihood of producing such organisms is by no means negligible if large amounts of streptomycin are given over long periods. Careful consideration must be given to this possibility, and the risk of performing a resection at an unduly early stage must be weighed against the risk of producing resistant bacilli.

A relatively high proportion (22%) of my resections have been performed to deal with disastrous A.P.s, often associated with bronchial stenosis.

TABLE II.—*Pneumothorax Disasters*

Total no. of resections	78
Resections of A.P. disasters	17
With only pathological evidence of stenosis	11
With bronchoscopic evidence of stenosis	6

In my opinion, for cases with definite bronchoscopic evidence of stenosis, except in the upper lobe, pulmonary resection should normally be preferred to initiating an A.P. Where it is not possible to prove stenosis bronchoscopically, any evidence that stenosis is probably in the middle lingula and lower lobes indicates that the A.P. should only be tried to provide evidence on the question; it should be continued only if no support is given to the suspicion; resection should be preferred if the suspicion is confirmed.

The use of pneumothorax is more debatable in cases of upper lobes with cavitation and occult bronchial obstruction. In some of these, cavity closures can be obtained with the production of a completely airless lobe, with a freely expanding lower lobe. Should these cases be submitted to lobectomy? Contrary to some workers, I believe that these are comparatively safe if two essentials are fulfilled. (1) The presence of a residual cavity must be excluded by every possible means; if it exists there is a likelihood of two disasters: (*a*) a pin-point broncho-pleural fistula with production of fluid; and (*b*) spread into other parts of the lung. (2) The atelectasis must be complete. If the atelectasis is of one segment only, there is a likelihood that periodic reinflation of the incompletely collapsed area may occur and thus, by altering the dynamics of the lung, lead to spreads to the other side. If the atelectasis of the upper lobe is complete, resection is unnecessary, at any rate at this stage, for reinflation should not occur. When re-expansion is allowed, the collapsed lobe will occupy a narrow wedge against the mediastinum at the apex, and this will result in a symptomless bronchiectasis. In the event of trouble the shrunken lobe can be removed subsequently. There are two objections to primary resection in these cases: (1) the middle and lower lobes are nearly always the seat of some disease, even though it is occult and the A.P. is very valuable in assisting to heal this; and (2) the availability of skilled surgeons for whom resection is a safe procedure is limited.

A very important point arises in connexion with cases in which a pneumothorax has been maintained for six months and upwards in the presence of an unclosed cavity. Before the advent of resection the physician was in rather a quandary. If he allowed re-expansion there was a great chance of spread of disease into other areas during the re-expansion of a lung which had been collapsed without cavity closure for some months; on the other hand, few surgeons liked the idea of performing a thoracoplasty without re-expansion owing to the danger of tearing the pleura. Resection obviates this difficulty.

The Residual Pulmonary Function

The estimation of the residual pulmonary function which will follow pneumonectomy is of course of primary importance: a patient who has severe dyspnoea on any exertion is a poor result. Some years ago Dr. Cheale and I investigated the capabilities of patients who had had lungs removed for bronchiectasis and carcinoma, taking ability to climb the stairs from the ground to the first floor without distress as our basis. We found that in young people who had had pneumonectomy for bronchiectasis, and in patients under late middle age who had had the operation performed for carcinoma, the function was usually remarkably good. The bad group was the middle-aged bronchiectatic. These included those who had damage from bronchitis and emphysema on the other side.

If the serial *x*-ray films in a case of pulmonary tuberculosis of long standing are studied the current film may appear comparatively normal, whereas the previous films

will show that a considerable amount of disease has been present and has radiologically disappeared. Post-mortem examinations, when available, indicate that the radiological clearing is not proof that quite extensive damage does not persist in the form of foci of chronic tuberculous pneumonia and fibrosis with emphysema and chronic bronchitis, which is often intermittently silent. Hence, before a lung resection of choice is embarked upon it is essential that all possible previous *x*-ray films or, if not available, reports, should be studied. This is often of more value than function tests, which I find rather disappointing in assessing the doubtful case.

In this series two patients died and two are respiratory cripples as the result of miscalculation of respiratory reserve, but only one was an operation of choice.

Reasons for Resection

I have divided the reasons for resection into three classes, but not by the pre-operative indications for it. I have taken the specimens removed and post-operative *x*-ray films —that is, I have, as they say on the Stock Exchange, "jobbed backwards" and considered the cases with the possible alternative methods of treatment thus revealed. (1) Where the alternative to resection was chronic invalidism with the prospect of early death (58 cases). (2) Where the alternative was some other form of major surgery (15 cases). (3) Where non-surgical treatment was possible (5 cases).

1. Resection or Chronic Invalidism

Under this heading we may include the following conditions: destroyed lungs or lobes, with cavitation; bronchial stenosis of the main bronchus or of the middle- or lower-lobe bronchi; cavitated and bronchiectatic lesions of the middle and lower lobes which have proved unamenable to other treatment; and cavitated lesions with empyemata or fistulae, especially after disastrous A.P.s.

In this group the problem is to assess the value of the patient's life to him, under the conditions prevailing at the time of the proposed operation and the prospects of rapid deterioration. Some of these cases may have years of useful though restricted life before them even if nothing is done. In assessing the risks of operation, careful review of the patient's previous immunological response to the tubercle bacillus is almost as important as the *x*-ray film; in addition, the fortitude which a patient has shown under previous misfortune will often allow his physician to encourage the surgeon to take a risk which on the face of it is too great.

2. Resection or Some Other Form of Major Surgery

Among my cases there were seven pneumonectomies in which a complete thoracoplasty would have been a possible alternative: these were cases in which cavitated fibrocaseous disease involved the whole lung without stenosis of the lower- and middle-lobe bronchus, or basal cavitation.

From the point of view of local condition there is no doubt that the pneumonectomy will give a better result. If the effect of distension of the other lung is feared a subsequent paravertebral thoracoplasty can be done with a minimum of risk, or, as in this type, if a pneumoperitoneum and a phrenic interruption can be done without disadvantage, this may suffice. I believe, however, that a thoracic surgeon of limited experience or with limited facilities may perform a staged thoracoplasty with less risk. We should not encourage the relatively inexperienced surgeon to abandon a well-established and comparatively safe operation for a method of treatment which is on trial. Apart from this, I think that a planned complete thoracoplasty is seldom called for.

In the other eight cases an upper-stage thoracoplasty would have been possible, and one of the most controversial questions is the respective advantages of the upper-stage thoracoplasty and resection in disease of the upper half of the lung.

From the point of view of function, all other things being the same, the functional result of an upper-lobe resection must be better than a seven-rib thoracoplasty, but if a pneumoperitoneum and a phrenic interruption are done to help to fill the space the advantage is negligible. The advocates of resection often advise inducing this quite casually; but the figures of Michael and others show that recovery of phrenic nerve function fails to occur in about 20% of cases in which a pneumoperitoneum is used to supplement the phrenic interruption, and partial lack of recovery is found in 30–50%. Where the thoracoplasty is confined to five ribs the difference must be much less, and an apical thoracoplasty has comparatively little effect on function.

I do not propose to go into the results of the complications of resection and thoracoplasty except to point out that a thoracoplasty avoids two difficulties that may occur in resection.

1. A lobectomy may be contemplated, but for technical reasons it may be found at operation that a pneumonectomy is essential. As experience is gained the possibility of this may be negligible, but at present there are cases in which it does occur. If the other lung is not sound the loss of a lobe which was relied on to make up a deficiency may be a serious thing. The functional result of a pneumonectomy will be inferior to that of a seven-rib thoracoplasty. The latter will preserve functioning lung, which will be of great value, especially if there is reactivation of disease in the other lung.

2. In dealing with cavities in the middle zone their exact location in cases in which much distortion has occurred is by no means easy, even when every facility is available. If the surgeon discovers at operation that an error in location has occurred a pneumonectomy may be necessary, with a corresponding diminution of available functioning lung.

In my series a pneumonectomy was performed in six cases in which the pathological specimen showed that the lower lobe was sacrificed when its condition was such that it would probably have healed. In three a pneumonectomy was performed deliberately, as it was thought that the condition of the lower lobe was worse than it was; in three a lobectomy would have been done if it had proved practicable. In all these a seven-rib thoracoplasty would probably have been successful and one death avoided.

This also raises a further point: some surgeons say that if they find that the condition of the lobes, other than the one which they propose to remove, is worse than the *x*-ray film suggests, they extend the resection. This seems to me quite wrong unless the film has been misinterpreted and a given shadow is not in the lobe in which it was envisaged.

If no lesion shows in the film there is no more reason why a similar amount of disease in the supposedly good lung would not be found if it were examined. The pathological condition is difficult to interpret at the operation till the lung is cut; and the patient's resistance may completely alter the picture.

The risks to life after an upper-stage thoracoplasty will of course vary enormously with the material which is operated, but unless desperate cases are tackled it is very low. Similar results in resection have been published by some workers, but my figures hardly bear this out; the onus lies on the advocates of resection to show that in a similar type of case such a low mortality can be obtained by the average thoracic surgeon. Until that is proved to be the case I think that it would be a grave error to assume that the very low figure published by some very brilliant surgeons, and the Liverpool School headed by Mr. Ronald Edwards in particular, will be produced by all other workers. I suspect that the difference lies in the type of material.

The problem is further complicated by the remarkably good immediate results obtained by some surgeons by the use of plastic ball plumbage. Even though it is suitable for only a proportion of cases to which the other procedures are applicable, it yet does provide an alternative to resection in some cases—for example, those in which the

possibility that a contemplated upper lobectomy may be a pneumonectomy, with the likelihood of disaster—while avoiding some of the disadvantages of a thoracoplasty.

It will be noted that so far I have not referred to the bearing of bronchial stenosis on upper-lobe disease. Bronchial stenosis, unless absolutely complete, which is comparatively uncommon, will almost certainly produce some bronchial dilatation. Is this important? If it is, all upper lobes in which narrowing of the bronchus can be diagnosed are cases for resection unless there is a definite contraindication. All one can say is that many cases in which upper-lobe bronchial dilatation, either under a thoracoplasty or produced by spontaneous healing, remains do very well for many years; the drainage is so good that a slight cough in the morning and sputum free from tubercle bacilli are the only symptoms of its presence. The dilatation can be demonstrated easily by bronchography, but the clinical effect is small. I feel that the few patients who do develop recurrent pyrexial attacks and in whom a lobectomy is subsequently necessary do not as yet tip the balance against a small thoracoplasty.

With the nervous and unstable patient there are great advantages in resection. It is one thing to screw up one's courage for a big operation; it is another to face two operations, as must be done when a thoracoplasty is contemplated. To a woman, especially a young unmarried woman, it is often the deformity produced by the falling in of the ribs and by the spinal curvature, even if these be minimal, which is the main horror of a thoracoplasty. The following case illustrates this point.

A woman aged 22, after a partially successful pneumothorax and a phrenic interruption, was left with a shrunken upper lobe with an infrequently bacilliferous cavity. A thoracoplasty was advised by a surgeon, who practically guaranteed a permanent arrest of the disease. Knowing the patient, the physician advised against it. The thoracoplasty was done with complete local success and closure of the cavity. She returned to her physician some time later as she had influenza, and she was doubtful about her condition. There was no recurrence of disease, but she looked ill. She was an alcoholic addict and had tried to commit suicide: she had become an alcoholic because she was so ashamed of her deformity (which was hardly noticeable) and she had cut herself off from all her friends and refused to go out. She attempted suicide when she heard that if she had waited she could have had a lobectomy without deformity of the chest wall. Her physician knew that a quiet life with a cavity and an intact thorax would have been a much better result than a closed cavity with a ruined life; he realized that her appearance was the breath of life to her.

3. Cases in Which Non-surgical Treatment was Possible

These were inspissated cavity (one), tuberculomata (two), and localized areas of fibrotic disease (two). In none had tubercle bacilli been demonstrated at the time of operation; in three no growth, and in two very scanty growth only, was obtained from the pathological specimens. Judging from the pathological specimens, conservative treatment would have been adequate in four and less disastrous in the other.

I am extremely doubtful whether resection is indicated in the absence of tubercle bacilli and symptoms of activity—that is, a static *x*-ray shadow, even if known to be tuberculous in origin, is not in itself an indication for resection.

Timing

The success of thoracoplasty has been largely attributable to the insistence that a good resistance is a *sine qua non*. This insistence must be applied to resection or the results will be poor in the long term. However, our estimation of resistance is fallible and largely dependent on the observation of the individual's reaction to the disease. This takes time. In the 78 cases under review 34 were known to have had tuberculosis for more than four years, 24 for two to four years, 13 for more than one year, and 7 for less than one year, but all may have had the disease for much longer. Three of the latter seven had localized disease, which indicated a good resistance; a fourth, from the type of disease, was of considerable standing. The remaining three were probably acute low-resistance types; they were kept in bed for a minimum of three months and taken on very slowly afterwards, but one has already relapsed.

It is difficult to prove that cases treated with long periods of rest prior to resection do better than those who receive early operation; my present opinion is that resection should usually be postponed until the maximum benefit has been achieved by conservative measures. It may be argued that this policy will lead to bronchogenic spreads; but Mitchell has shown that in cavitated cases treated by phrenic interruption and rest in bed this seldom occurs.

The Contralateral Lung

Passing to the effect of lung resection on the other lung, there are three points which I should like to consider. (1) What is the effect of removal of a mass of tuberculous tissue on the other lung from the point of view of immunity? (2) What is the effect of overdistension on the tuberculous foci, which must be assumed to be present even if not radiologically evident, in the contralateral lung, or in the remainder of the lung in the resected side, when a subtotal resection is performed? (3) Is deterioration in the contralateral lung likely after the patient has recovered from the immediate effects of the operation?

1. It is obvious that the removal of a source of bronchogenic spread must reduce the chance of such a spread; but it is not so clear whether the presence of tubercle bacilli in the right number in the body may not keep up the acquired immunity, although I think that there must be adequate numbers elsewhere to deal with this. In some cases, however, the basic cause of the disease is haematogenous in spite of the fact that the main lesion in the lungs is a bronchogenic lesion which is superimposed. It has been found that in extrapulmonary tuberculosis the removal of the principal focus may be followed by recrudescence of disease elsewhere, and that if a pulmonary case is mainly haematogenous it is possible that this may occur in the lungs. However, it may be said that so far there is no real evidence that pulmonary resection will have an adverse effect on the patient's immunity.

2. On the basis that relaxation is the method by which healing in the lungs can be promoted, overdistension should produce an adverse effect. However, comparison with a pneumothorax affords a possible explanation why this should not be so adverse in its effect as might be expected. When a lung free of adhesions is fully collapsed and then allowed to re-expand partially, the undiseased part re-expands more readily than the diseased area owing to its unimpaired elasticity: this is the mechanism by which selective collapse is produced. By analogy it may be that the overdistension falls mainly on the undiseased part of the lung with little effect on the diseased area.

3. A review of these cases shows that 7 out of the 70 survivors (10%) showed some evidence of deterioration in the two years following the operation. Two factors seemed to be of importance. (i) Deterioration took place five times as frequently in those cases in which there had been adverse changes in the contralateral lung during the previous 12 months as in those in which there was no previous or only static disease. (ii) Deterioration was more frequent in patients who were over 50 at the time of operation. The details of this investigation will appear in *Thorax*.

Results

The mortality from lung resection will vary very much with the type of case which the physician and surgeon agree is a possible risk. Where the alternative is chronic invalidism or the likelihood of early death, it is justifiable to tackle cases with a high mortality risk; and a high mortality in this class of case throws no reflection on the surgeon and little on the physician.

The results are shown in Table III ("satisfactory" indicates that the disease is apparently arrested and no tubercle bacilli are found in the sputum). In the group where resection was the only possible method of treatment 64% can be classified as satisfactory, 15% were dead, and 21% unsatisfactory. Where alternative surgical treatment was possible 80% were satisfactory, 7% dead, and 13% unsatisfactory.

TABLE III.—*Results*

	Satisfactory	Unsatisfactory	Died	Total
No alternative treatment:				
Pneumonectomy	25 } 37	8 } 12	7 } 9	40 } 58
Lobectomy	12 }	4 }	2 }	18 }
Surgical alternative possible:				
Pneumonectomy	4 } 12	1 } 2	— } 1	5 } 15
Lobectomy	8 }	1 }	1 }	10 }
Conservative treatment possible:				
Pneumonectomy		1		1 } 5
Lobectomy	4			4 }
Totals	53	15	10	78

Causes of Death.—Table IV shows the causes of death. In four cases the surgeon did not have a chance—in two the respiratory reserve was too low, but in both the possibility was recognized before operation; in the other two the operation was satisfactory, but the patients' resistance was not sufficient to deal with the remaining disease.

TABLE IV.—*Causes of Death*

Operative deaths	6
Lack of respiratory reserve	2
Directly following operation	2
Blood-transfusion disaster	1
Oedema of larynx	1
Post-operative deaths (failure of treatment)	

Unsatisfactory Results.—In 15 cases classified as unsatisfactory the patients were still alive at the end of the period of observation. Three cases are in serious danger, and one is well except for a small sinus. Of the others the deterioration on the other side is slight in four cases, and there is a reasonable prospect that it will settle down.

TABLE V.—*Unsatisfactory Results*

Pneumonectomy (obligatory)	8	Pneumonectomy (choice)	1
Persistent sinus	1	Deterioration other lung	1
Deterioration other lung	4		
T.B.+; ? cause	1		
Respiratory cripples	2		
Lobectomy (obligatory)	4	Lobectomy (choice)	1
Deterioration other lung	1	T.B.+ same lung	1
T.B.+; cause ?	1		
Spread other lung	2		
For Localized Disease: Pneumonectomy			
Deterioration other lung	1		

Conclusions

Any investigator into the results of and indications for any particular mechanical form of treatment for pulmonary tuberculosis is confronted with the difficulty that if he allows a long enough time to elapse to enable him to reach a definite conclusion the method of treatment may have improved so much that the immediate mortality figures are out of date. In all probability the mortality figures obtained here would be reduced if the operations were performed to-day; but if advanced cases are tackled the mortality will be appreciable. Most cases dealt with have been followed for a minimum of two years.

It can be claimed, however, that this paper does confirm the opinion that in resection we have a method by which many cases unsuitable for any other form of surgical treatment can be rendered quiescent; a high proportion (64% of 58 cases) who would be dead or hopeless invalids have been rendered quiescent with a good prospect of ultimate arrest of the disease. Resection has not yet proved itself superior to surgical collapse therapy in upper-zone disease.

The cases dealt with are mainly those which have shown a fair degree of resistance, and the findings are not applicable to cases in which the disease is recent in onset. The basic indication for resection in advanced cases is bronchial stenosis or its results.

As the cases were selected for operation by a number of physicians and include cases operated on by at least five surgeons the results may be regarded as representative of average high-class clinical work. The cases are not confined to one particular type.

It appears that if deterioration is going to occur in the opposite lung it will probably do so within a year of the start of convalescence. The likelihood of deterioration is high where the disease has shown signs of instability within the previous year or in patients over 50 years of age.

I acknowledge with gratitude the kindness of my colleagues at Brompton Hospital, who have allowed me to use their case notes and radiographs. The accuracy and success of the follow-up are entirely due to my registrar, Dr. M. R. Geake, to whom I tender my warm thanks.

SKIN LESIONS IN ORGANIC BRAIN DISEASE

BY

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During recent years many papers have been published on the psychological aspects of skin disease, yet comparatively little has been written on the subject of skin lesions found in association with organic brain disease. This discrepancy has not passed unnoticed by dermatologists, and MacKenna (1947) has commented on it in his introduction to Wittkower's article on the psychological aspects of seborrhoeic dermatitis. Posing the question, "To what degree does the mind influence the behaviour of the skin and its appendages?" he points out that the answer must concern itself with the cerebral control of the epidermis, and goes on to state that "a search of the literature indicates that from the dermatological standpoint there have not been any great advances since D. Krestin published his famous paper on 'The Seborrhoeic Facies as a Manifestation of Post-encephalitic Parkinsonism and Allied Disorders.'" Krestin's paper was published in 1927, and on the basis of 73 cases studied in the wards of the London Hospital he made the suggestion that the secretory disturbances described might "depend upon lesions in the neighbourhood of the third ventricle involving vegetative nerve centres."

More recent evidence that cerebral lesions can be followed by skin changes has emerged from the study of patients subjected to prefrontal leucotomy. Ziegler and Osgood (1945), in a careful study of the post-operative findings in 17 patients submitted to leucotomy, found that three suffered for a variable period post-operatively from a bullous eruption of the heels. These bullae healed slowly and were stated "to resemble

trophic ulcers in every way." No fewer than seven of their patients showed bilateral oedema of the legs and feet, and in these seven were included two of the three patients exhibiting bullae. All the patients showing oedema and/or bullous eruptions survived, so there was no necropsy evidence of the exact location of the leucotomy lesion in these cases. It is known, of course, that the cerebral course traversed by the leucotome at the operation of prefrontal leucotomy can vary widely from case to case (Meyer and Beck, 1945), and clinico-pathological correlation derived from a comparative study of the brains of patients dying some time after the operation has already yielded valuable information in relation to cerebral anatomy and cerebral function (Meyer, Beck, and McLardy, 1947 ; Meyer and McLardy, 1948, 1949).

A paper by McLardy (1950) deals more specifically with the necropsy findings in cases showing skin lesions following leucotomy. Analysing a series of 122 cases of post-leucotomy deaths, in which the time interval between operation and death ranged from five hours to five and a half years, McLardy segregated 14 cases which appeared to him to form a homogeneous group. The post-operative period of survival in these 14 cases was never less than five weeks or more than six months. He considered that all were "delayed post-operative deaths," the putative cause being "trophic deterioration." Of this group of 14, seven showed "remarkable similarity," in that they all became marasmic and died with multiple cutaneous septic sores within two to five months of operation, and, moreover, the area of the brain transected by the leucotome in these seven cases was roughly similar.

The cases here reported concern four female patients suffering from some form of organic cerebral disease who developed skin lesions prior to death. (Two cases with cutaneous manifestations limited to the sacral area and heels have been discarded, since in these it was impossible to assess the part played by such factors as pressure and inanition.) In three of the four cases described the cerebral lesion was extensive ; they therefore lack the localizing value of the circumscribed leucotomy transection. Nevertheless, in view of the few clinical reports extant on the subject of the cerebral control of the epidermis, the description of these four cases may be of value.

The accounts of the clinical examinations and necropsy findings are considerably abridged for reasons of space.

Case 1

Diagnosis : Glioblastoma

A married woman aged 68 was admitted on December 21, 1946. The first deviation from normal was noted 15 days before admission, when she was seen to repeat the process of preparing the house for the annual chimney-cleaning, although this had actually been carried out the previous day. Subsequently she showed a progressive failure in comprehension and practical ability. She was often incontinent.

Examination.—The patient was an elderly woman of healthy appearance, who walked into hospital. Detailed examination of the C.N.S. revealed no focal neurological signs in the somatic sphere. C.S.F.: normal pressure and constituents. In the mental sphere she showed marked defects of an aphasic and apractic type. Her mood was one of mild euphoria: she punctuated her remarks with smiles and was obviously unaware of her situation. A gross intellectual deterioration of such rapid onset, with no antecedent history of trauma or illness, made it reasonably certain that the underlying condition was that of a malignant tumour.

Skin Lesions.—Six days after admission, when the patient was still ambulant, a small abrasion was noted on the skin overlying the coccyx. Two days later a bullous lesion, resembling a second-degree burn, appeared in the same area. This extended rapidly during the course of a few hours, until both buttocks and the posterior aspects of both thighs were involved. During the next few days bullous eruptions appeared on both legs and feet. Sloughing quickly occurred in those areas submitted to pressure. Death occurred on January 8, 1947, 12 days from the date of the appearance of the bullae.

Necropsy Report

The presence of a cerebral tumour was confirmed, and histological examination showed this to be a glioblastoma multiforme. The bulk of the tumour lay in the base of the left hemisphere, extending from the frontal pole into the temporal lobe as far back as the level of the corpora mammillaria. It crossed the midline, however, to invade the base of the right frontal lobe and therefore gave the impression of a midline growth. At the level of the anterior horn the tumour extended to invade the left side of the corpus callosum. It compressed and displaced upwards the left lateral ventricle, while the right lateral ventricle was displaced to the right and dilated. A cyst was present in the right frontal lobe on the lateral aspect of the tumour. The tumour reached the surface anterior to the infundibulum, invading both gyri recti, surrounding the optic chiasma and nerves and left middle cerebral artery. Apart from small foci of recent infarction in both lungs, no abnormalities were detected in the other organs.

Case 2

Diagnosis : Carbon Monoxide Poisoning

A spinster aged 63 was admitted on January 2, 1948. Four weeks previously she had been admitted to a general hospital following an attempt at suicide by the inhalation of coal gas.

Examination.—A few small pustules were present on the right elbow. B.P. 150/90. No focal neurological signs elicited. Gait unsteady on rising from chair but improved on walking. C.S.F., negative. W.R., negative. W.B.C., 6,000. Mental testing showed severe memory defects and disorientation for time and place. It was obvious that a severe degree of cerebral damage had occurred as a result of prolonged exposure to coal gas.

Skin Lesions.—On January 7 the patient developed an acute rapidly advancing bullous eruption over the sacral region and buttocks. Penicillin therapy was instituted, and over the next ten days her general condition improved and the bullous eruption appeared to be healing. On January 18 she again relapsed, and from this date to her death on January 22 her temperature showed a stepladder rise each night and the bullous eruption over the sacrum spread upward over the lumbar and dorsal vertebrae. Fresh bullous eruptions appeared over the right scapula, the antero-medial aspects of both legs, and right heel. (These bullae had all the appearance of superficial burns, and in fact those over the anterior aspect of both legs were referred to as such in the necropsy report.)

Necropsy Report

Sections of the brain were examined from all regions. The cortex showed loss and degeneration of nerve cells. In the white matter there were numerous irregular areas of demyelinization of varying size and shape which were diffusely infiltrated by cerebral histiocytes containing much fat. Similar areas were present in the basal ganglia. The features were those of a typical case of subacute/chronic carbon monoxide poisoning showing active demyelinization in white matter. Toxic changes were noted in heart, liver, and kidneys.

Case 3

Diagnosis: (1) *Dermatitis Gangrenosa of Left Lower Limb Following Severe Pemphigus;* (2) *Subdural Haematoma Overlying Right Cerebral Hemisphere;* (3) *Depressive Psychosis*

A married woman aged 53 was sent into hospital on August 15, 1946, as a case of involutional depression. Examination, however, revealed that she was suffering from an organic cerebral condition with focal neurological signs and intellectual defects. Her relatives stated that six weeks previously she suddenly complained of intense headache over the right temple and thereafter lapsed into a "drowsy state," with incontinence. She reiterated questions regarding her husband and son—seemingly unaware that her husband had died two years previously. After two weeks she was admitted to a nursing-home. In her waking periods she showed understanding of questions and answered them correctly, although a minute or so later she forgot both the question and her reply. Later a depressive thought content became manifest—characterized by ideas of guilt and unworthiness; and after four weeks in the nursing-home it was judged necessary to admit her to a mental hospital.

Physical examination on admission showed:—C.N.S. (positive findings only): knee-jerks diminished on both sides; ankle-jerk diminished on right, absent on left. Bilateral extensor plantar response. A generalized hyperaesthesia to pinprick was present on admission and for three days thereafter. The C.S.F. was under normal pressure; protein, 75 mg. per 100 ml.; globulin, slight increase; cells, 1 per c.mm.; W.R. negative; colloidal gold, 0011000000; blood chemistry normal. Radiological examination of skull and chest negative.

Mental examination showed that she could answer simple questions about herself, but was unable to deal with questions requiring reasoning and calculation. She appreciated to some extent her intellectual disability. She had an amnesia for the previous four weeks. Her speech was slow, her voice monotonous, her response retarded. She yawned often during interrogation and made smacking movements with her lips.

After-course of Illness.—At the end of two weeks she had largely regained her mental clarity. C.S.F. protein, however, rose to 110 mg. per 100 ml. As her intellectual defects disappeared her depressive thought content became more prominent. On September 28 she was sent for more detailed neurological investigation, but this failed to reveal any lesion which could explain the original illness and the residual focal sign of bilateral extensor plantar response. On January 23, 1947, the C.S.F. protein gave a normal reading of 35 mg. per 100 ml. During the next eight months her condition remained static. She had regained her normal intellectual standard—so far as this could be assessed—although she was amnesic for the early period of her illness. The plantar response remained extensor. She was still deeply depressed. Electric convulsion therapy, which might have relieved the depression, was contraindicated because of doubt concerning the exact nature of the cerebral lesion. Her physical condition was satisfactory and she occupied herself in daily domestic tasks in the ward.

Skin Lesions.—On October 29, 1947—that is, 14 months after admission—a widespread bullous eruption developed with dramatic suddenness over a wide area on the inner aspect of the left thigh and anterior surface of the left leg. The bullae varied in size, contained yellow serum, and had the appearance of an acute pemphigus. A minute crop of bullae appeared transiently over the left forearm. Her temperature rose to 99° F. (37.2°C.) on the day on which the eruption first appeared, but thereafter the temperature and pulse rate were normal until the terminal week of the illness. During the next four weeks the subcutaneous tissue in these affected areas progressively sloughed, so that the underlying muscles were clearly visible. At the same time, bullae appeared progressively in neighbouring areas, so that finally the entire surface of the left lower limb, with the exception of a narrow strip on the posterior aspect of the limb and the sole of the foot, was involved in the eruption. In course of time erosion of the subcutaneous tissue occurred also in these later affected areas so that the final appearance was that of a widespread dermatitis gangrenosa. Blood transfusion and every variety of antibiotic were utilized throughout the long course of the illness. In the third month granulations appeared in some of the areas affected, but coincidentally the dorsum of the foot became grossly infected—the infecting organisms being resistant to penicillin. The patient now looked extremely toxic and had fluctuating oedema of the face and sacrum. In the terminal phase hydrothorax developed. Death occurred on February 27, 1948, four months after the first appearance of the skin lesions.

Necropsy Report

General Appearances.—The whole of the left leg was involved by an extensive and severe ulcerative process involving skin and subcutaneous tissue, and in places extending down to the underlying muscle. Some of the ulcers, especially those on the anterior aspect of the tibia, were healing well by granulation and were relatively free from infection, but others showed little or no sign of repair and were grossly infected.

Brain After Fixation.—Macroscopically, the inner layer of dura over the right frontal lobe on its supero-lateral aspect was discoloured with blood pigment and showed on its cortical surface "neomembrane," suggesting that at some previous date there had been a subdural haematoma which had since become absorbed. Microscopically, a section from the dural lesion showed that the inner aspect of dura was almost continuously lined by a thin layer of golden-brown haemosiderin pigment which lay mainly extracellularly. The "neomembrane" seen with the naked eye consisted of loose fibrovascular tissue with similar pigment deposits scattered within its substance. A section from basal ganglia revealed no striking abnormalities except for a few small irregular cystic spaces formed by degenerative changes in the neuroglia, probably of a chronic ischaemic nature. Findings in other organs were: right hydrothorax, partial collapse of lower lobe of left lung, "septic" spleen, and periportal fatty degeneration of liver cells.

Case 4

Diagnosis: Chronic Mania; Subdural Haematoma

This case differs from the previous three cases in that the skin lesion was not a bullous eruption. It also differs in that the patient had been in hospital for many years suffering from a long-term mental illness.

A spinster aged 42 was admitted on March 27, 1922. With advancing age her psychotic illness had rendered her uncommunicative, and accurate intellectual assessment was impossible. For two years she had been confined to bed because of a fractured neck of the femur.

Skin Lesions.—On November 10, 1950, she developed a slight rash on the face, and this erythematous rash later spread to involve her whole body. The upper and lower limbs were most severely affected, and the skin in these regions developed a shiny bright-red appearance with numerous petechial haemorrhages. Finally, the lower limbs became oedematous and bright purple in colour, and small areas of gangrene appeared over the heels and soles.

It was at first thought that the dermatitis was due to drug sensitivity, but when exacerbation and not amelioration followed the prohibition of the very small doses of drugs administered at infrequent intervals, and to which she had not previously shown intolerance, an organic cerebral lesion was suspected—largely on the basis of the knowledge gained from the foregoing three cases. The patient died on December 6, 1950, at the age of 70.

Necropsy Report

Brain After Fixation.—The dura: large subdural haematomata covered the supero-lateral surfaces of both hemispheres. On each side the haemorrhage was limited on its inner aspect by a well-defined thin membrane which extended over the entire haemorrhagic area and enclosed within itself and the dura several ounces of blood clot. External examination of cerebral hemispheres showed considerable flattening and compression from side to side of the right hemisphere, most pronounced in the fronto-parietal region. Microscopically the inner aspect of the dura covering the haematoma showed a well-defined layer of granulation tissue containing abundant haemosiderin pigment lying free or in histiocytes. Collagen fibril formation was well marked and proliferating capillaries were prominent. Sections were taken of the frontal cortex near the tip of the anterior horn. No pathological changes were noted.

Other Organs.—Skin lesions: the superficial layers of the dermis were swollen and oedematous and showed focal collagen degeneration. There was a fair degree of inflammatory cell infiltration, the majority of the cells were lymphocytes, but pyknotic polymorphs and histiocytes were also present. The capillary walls were swollen and in many places showed proliferation. Diffuse haemorrhage was present. The overlying epidermis showed degenerative changes. Eosinophil polymorphs were found in small numbers throughout the inflammatory infiltration. Lungs: pneumonic consolidation was present in both lower lobes. In addition, many of the small vessels showed both periarteritis and mesarteritis, the inflammatory cells being mainly polymorphs. This vasculitis was probably distinct from the pneumonic process.

Review of Literature

Apart from the trophic skin lesions described in post-leucotomy cases, there are few published reports of cutaneous disturbances in cerebral disease. Bullous eruptions have been described very occasionally as a concomitant of epidemic encephalitis. Stern (1936) states: "The origin of the trophic changes of the skin and joints found in occasional cases remains inexplicable. Gangrene and blisters on the hands have been described in both acute and chronic stages of the disease. . . . I personally have seen a severe case of chronic Parkinsonian encephalitis in which there occurred simultaneously a *pemphigus-like* disease. Whether there is any connexion between the two diseases is open to discussion." Rostowski (1939) has drawn attention to the "almost invariable" occurrence of bullous eruptions in "choreiform" encephalitis—"the parts most commonly affected being the circumoral region, the chin, the skin overlying the elbows and knuckles. The lesion commences as erythematous patches on which develop small or large vesicles containing first white and later yellow fluid. These vesicles enlarge and coalesce, ultimately rupture, and leave wounds which are difficult to heal." This author believes that "it is the cerebral infection which accounts for the skin lesion, and not the trauma to the skin resulting from the choreiform movements. That this is so is proved by the finding that such eruptions have never been seen in Sydenham's chorea, although the ceaseless movements may be of the same intensity as that seen in choreiform encephalitis" (Rostowski, personal communication).

More numerous, but still far from frequent, are the reports of bullous eruptions accompanying spinal-cord lesions. Cutaneous bullae are, of course, mentioned in textbook descriptions of myelitis and syringomyelia as occasional concomitants of these diseases, in which it is usually assumed that they are secondary to the sensory changes. Some authors believe, however, that these bullous eruptions, which so often resemble pemphigus in appearance, are the results of impaired skin nutrition, and are primary "trophic" changes, in the sense that the spinal-cord lesion causes at one and the same time alterations in skin sensibility and in skin nutrition.

A typical report of this kind is that of Milian and Lelong (1922), and concerns a man of 66, with a syringomyelia of eleven years' duration, who had thrice had a "pemphigoid" eruption. The eruption was bilateral and symmetrical. On the third occasion the bullae were distributed over the anterior and posterior aspects of both forearms. The authors regarded these bullae as trophic in origin because they were localized to areas "which showed the maximum atrophy and sensory disturbance," and considered that they were due to involvement of the grey matter of the spinal cord, particularly those areas containing the sympathetic centres of the trunk and limbs. They were careful to point out that, although a myelopathic pathogenesis was the most likely one in their case, this did not necessarily apply in all cases of pemphigus. Again, Ormsby and Montgomery (1948), in assessing the evidence for and against a neuropathic aetiology of pemphigus, mention that pemphigus has been observed in patients with neurogenic conditions, and enumerate various reported cases in which lesions of the spinal roots and/or spinal cord have been found at necropsy. These few scattered references therefore suggest the possibility that bullous eruptions may arise from destruction of either cerebral or spinal-cord centres.

Cerebral Localization.—A determined attempt has been made by McLardy (1950) to delimit a particular area of the brain, damage to which might be held responsible for the appearance of cutaneous blisters and marasmus in a group of patients dying within two to five months of the operation of prefrontal leucotomy. His examination (mainly macroscopic) of the brains of seven such patients revealed that in each the operation had caused bilateral damage to the subcallosal fasciculus at the level of the head of the caudate nucleus. He also found associated damage to other areas—notably (*a*) the striatum (under which term he includes the caudate nucleus and putamen), and (*b*) the cortex and digital white matter of the superior frontal gyrus at the topographical level of Brodmann's (dysgranular) area 8 and (agranular) area 6—but quantitative destruction of these regions varied from case to case. From his findings in these seven cases, and also from evidence supplied by other relevant cases in a total series of 122 necropsies in patients dying after leucotomy, he constructs the hypothesis that the three cerebral regions enumerated contribute to a connected vital system—"a vital fronto-subcalloso-caudate system"—disruption of which is responsible for the fatal "trophic deterioration." His hypothesis stresses the subcallosal fasciculus as the most important component in this system, since it presumes that this fasciculus, in its rostral portion at least, mediates connexions between the caudate nucleus and Brodmann's cortical areas 8 and 6.

Discussion

During the period 1946–51 more than 200 patients with one or other form of organic cerebral disease were under observation in this particular female section of the hospital. The four cases described represent only a small fraction of the total organic cases, indicating that such severe cutaneous manifestations occur infrequently. It is easy to visualize how such skin lesions may be accepted as merely a terminal manifestation of inanition occurring in bed-ridden patients. It is therefore of interest to note that three of the cases here described were ambulant and in an apparently normal state of nutrition when the skin lesions first appeared; the fourth, although confined to bed, was capable of active movements and appeared in good physical health.

The first three cases form a homogeneous group in that the skin lesion presented initially as a bullous eruption. In Case 1 (cerebral tumour) and Case 2 (carbon monoxide poisoning) the cerebral destruction was massive and rapidly progressive, and the skin eruptions were likewise of brief

duration, death occurring within two to three weeks of the first appearance of the bullae. Death in these cases was presumably caused by the cerebral lesion, the skin eruptions being only a minor contributing factor. Conversely, in Case 3 (subdural haematoma), in which the cerebral lesion was more circumscribed and, if one may so describe it, less "lethal," the skin condition ran a prolonged course of exactly four months, during which time it showed both recrudescences and attempts at healing. The death of the patient, which occurred at the end of this time, was almost certainly due to toxaemia and alterations in blood chemistry brought about by the extensive dermatitis gangrenosa of the left lower limb. The cerebral lesion was culpable only in a secondary sense, in that it is here postulated as initiating the skin condition.

This case is worthy of more detailed study. The subdural haematoma covered the supero-lateral surface of the whole right frontal lobe. Its onset presumably coincided with the symptom of intense headache experienced by the patient four weeks before admission to hospital. Its presence explained the intellectual defects and neurological focal signs elicited following admission. There was no history of trauma, but subdural haematoma often appears without recognizable antecedent injury. Considered in retrospect, the history of fluctuating drowsiness and confusion elicited on admission was typical of that found in subdural haematoma. The left extensor plantar response can be explained in terms of pressure on the right motor area. The right extensor plantar response, which is also present, suggests transmitted pressure to the left crus, and was therefore in the nature of a false localizing sign. Aird (1949) mentions that homolateral paresis or anaesthesia occurs in 30% of cases of subdural haematoma, because extracerebral lesions are more prone to push the contralateral crus cerebri against the tentorium. This bilateral extensor response was still present when the skin eruptions first made their appearance, although nearly sixteen months had then elapsed from the time of the acute symptoms of headache and fluctuating drowsiness, so that the subdural haematoma was still at this later period exerting intracranial effects. Nevertheless, if it is submitted that the cerebral lesion was in some way associated with the skin condition in this as in the two previous cases, the question must inevitably be raised of why the skin effects appeared after a latent period of sixteen months. The evidence, from similar skin eruptions in epidemic encephalitis, which were stated to arise at varying times in the course of the disease, partly answers this question. A more relevant reply is that subdural haematoma remains a mysterious condition, subject to curious exacerbations and remissions which are usually explained in terms of secondary haemorrhage within the original haematoma.

The fact that the subdural haematoma was found at necropsy in a state of almost complete resolution, with only membrane formation to testify to its former existence, can be utilized to explain the protracted course of the skin condition; for, assuming that the subdural haematoma was responsible for initiating the skin eruption and destruction of subcutaneous tissue, its own absorption would tend to allow of attempts at healing, such attempts presumably being rendered ineffective because of secondary infection and toxic absorption from the very extensive denuded surface. An even more cogent reason for assuming that the subdural haematoma was responsible for the cutaneous manifestations in this case is that those manifestations were confined to the contralateral side of the body. The subdural haematoma overlay the right frontal lobe, the bullous eruption appeared on the left lower limb (with an initial short-lived eruption on the left arm), and never at any time appeared, even sporadically, on the limbs or trunk of the right side. Since in all the other cases a bilateral cerebral lesion was found in association with a bilateral skin lesion, it is difficult to avoid the inference from this one case of unilateral distribution that the cerebral and cutaneous lesions are in some way connected.

Case 4 is considered briefly. Here the skin lesion did not appear as bullae but as a generalized erythema with petechial haemorrhages. In this case the presence of a cerebral lesion was suspected, although no neurological focal signs were present and the mental state of the patient was such that she could not be examined for possible intellectual defects. This diagnosis was made on the skin condition alone, largely as a result of knowledge gained from the first three cases. This patient died shortly after the publication of McLardy's report on the cerebral findings in patients dying of "trophic deterioration," and therefore at necropsy the area round the anterior horn of the lateral ventricle was carefully examined microscopically, but no abnormality was found. Examination of this particular area in the previous case of unilateral subdural haematoma (Case 3) similarly revealed no abnormality, but the examination was not so detailed as in Case 4. It would seem, therefore, that skin lesions can arise without damage to the subcallosal fasciculus.

Conclusions

In the cases described above, three types of cerebral pathology—namely, tumour, carbon monoxide poisoning, and subdural haematoma—were found in association with cutaneous bullae. Bullous eruptions have been previously described in epidemic encephalitis and as a sequel to the operation of prefrontal leucotomy. It would seem, therefore, that varying types of cerebral pathology can produce the same cutaneous lesion.

The cases described are too few in number and the disease process too diffuse to allow of any postulation in regard to the cerebral area mediating the skin changes. The main intention of this paper is to draw attention to this association between organic cerebral disease and skin lesions, now that similar phenomena have been described and investigated in relation to prefrontal leucotomy.

I wish to thank Professor Sir David Henderson for permission to publish these four cases. My thanks are also due to Professor A. M. Drennan and his associates in the Edinburgh University Pathology Department for the necropsy reports, and to Dr. S. A. K. Karagulla for the notes in Case 1. I am particularly indebted to Dr. Grant Peterkin, consultant dermatologist, for his interest and advice in this investigation.

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With the assistance of the Public Health Laboratory Service, the Veterinary Investigation Department (Ministry of Agriculture and Fisheries), and veterinary investigation officers in Scotland, the Laboratory Animals Bureau has made arrangements to provide all accredited guinea-pig breeders with a local diagnostic and advisory service. Each breeder is allotted to one, or sometimes more than one, near-by laboratory and instructed to send there for bacteriological examination all his guinea-pigs which die. The laboratory undertakes to examine the dead animals in order to discover the cause of death, to visit the breeder if necessary, and to advise on any prophylactic measures to be taken. The Bureau receives a duplicate laboratory report, and is thus able to take any further steps which may be indicated.

EFFECT OF ISONIAZID ON CARBOHYDRATE METABOLISM IN CONTROLS AND DIABETICS

BY

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Following the observation that reducing substances were present in the urine of 5 out of 24 tuberculous patients receiving *iso*nicotinic acid hydrazide (isoniazid) it was decided to investigate the nature of this reducing substance and whether isoniazid had any influence on carbohydrate metabolism. The literature contains few references to isoniazid as a reducing substance. In a report on the current status of isoniazid in the treatment of tuberculosis by the Executive Committee of the American Trudeau Society (1952) mention is made of the presence of traces of reducing substances in the urine. Their presence was not found by Benson, Stefko, and Roe (1952) or by Rubin, Lee Hassert, Thomas, and Burke (1952) in animals, nor by Robitzek and Selikoff (1952) or Elmendorf, Cawthon, Muschenheim, and McDermott (1952) in man. Selikoff and Robitzek (1952), however, mention the presence of reducing substance in the urine on one or two occasions in their series of 92 patients, but do not discuss the significance of this finding. Isoniazid contains in its molecule a hydrazine residue which provides it with a two-fold action—a reducing action and the property of combining with sugars and forming hydrazones and osazones. Preziosi (1952) reports on the interference between isoniazid and sugars in the Hagedorn and Jensen method of estimation.

Compounds chemically similar to isoniazid and other substances have been found to have an effect on carbohydrate metabolism. Izume and Lewis (1926) reported that hydrazine derivatives induce hypoglycaemia by injuring the liver and thereby interfering with the formation of liver glycogen. In addition, hydrazine, being a reducing substance, causes the urine to reduce copper solutions. Alloxan and allied compounds induce immediate hypoglycaemia associated with hepatic, renal, and pancreatic islet cell damage followed by permanent diabetes according to the extent of pancreatic islet beta-cell destruction induced (Dunn, Sheehan, and McLetchie, 1943; Koref, Vargas, Rodriguez, and Telchi, 1944). It is interesting to note that Sollmann (1948) reports that after large doses of morphine the urine often contains reducing substances which are partly morphine-glycuronic acid and partly dextrose, and that clinical doses raise the blood sugar for some hours in 10–15% of fasting individuals. This response disappears in a few weeks if the administration is continued.

Method of Investigation

The oral glucose-tolerance test was used to investigate whether isoniazid produced any disturbance in carbohydrate metabolism. The investigation was carried out in two groups of tuberculous patients, the first group consisting of six non-diabetics to serve as "controls" and the second of six diabetics. In these 12 patients the pulmonary tuberculosis was quiescent in three and chronic in three of each group. The following tests were carried out on each patient.

Test A: an Oral Glucose-tolerance Test.—Blood-sugar levels were estimated at 0, ½, 1, 1½, 2, 2½, and 3 hours. Urines were examined qualitatively for reducing substances at ½, ¾, 1¼, 1¾, 2¼, 2¾, and 3¼ hours. The urine samples were collected at mid-points between blood samples. The test was extended from the usual two hours to three hours, so that mild diabetic trends indicated by a failure of the blood sugar to return towards normal levels, if present, could be detected. Isoniazid was then given to each patient for the next seven days.

Test B: an Oral Glucose-tolerance Test Performed after Three Days on Isoniazid.—The patients were given a dose of 5 mg. per kg. body weight and the total daily dose was divided into two equal doses administered orally at 12-hour intervals. The test began at 9 a.m., and the first dose of isoniazid for the day was given at 8 a.m.—that is, one hour before the glucose-tolerance test was started, to ensure maximal blood level of the drug. Blood and urine samples were collected at the same times as for test A. The blood plasma isoniazid levels were determined at one and a half hours after the drug was given—that is, half an hour after the start of the glucose-tolerance test—after both two and three days of isoniazid administration, to confirm that blood levels of the usual therapeutic order could be expected.

Test C: a Fasting Tolerance Test Performed After Six Days on Isoniazid.—Blood and urine samples were collected at the same times as for tests A and B, but no glucose was given. The blood plasma isoniazid levels were determined one and a half hours after isoniazid was administered.

The preparation of patients for tests A and B was as follows. The last meal was taken at 7 p.m. on the night before the test. Nothing else was eaten or drunk overnight. First thing in the morning on waking—that is, three hours before the test—a cup of weak tea with no milk or sugar was allowed. For the glucose-tolerance test 50 g. of glucose dissolved in 150 ml. of water was administered, followed by 100 ml. of water to remove the sweet taste. Blood and urine samples were collected at the times stated, with urines arranged so that blood samples were at the mid-points of urine collections.

Blood sugars were estimated from venous blood by the Folin–Wu method. Urines were examined by Benedict's method for reducing substances. If reducing substances were present their identification was attempted. Osazone tests and sugar chromatographic studies were carried out. Blood plasma isoniazid levels were estimated by the method described by Mueller and Fox (1951).

All of the six diabetics were on a mixed dose of soluble insulin and protamine zinc insulin prior to the tests, but for a week before and during the trial the P.Z.I. was discontinued and S.I. alone was given morning and evening. On the days of tests A, B, and C the morning insulin was not given until after the tests had been completed.

Results of Investigation

Dosage and Plasma Levels of Isoniazid.—The dosage and plasma levels in the controls and diabetics are presented in Table I. The total daily dosage of isoniazid varied between 250 and 425 mg. for the controls, with an average of 312.5 mg. and between 300 and 400 mg. for the diabetics, with an average of 334 mg. These doses are higher than those recommended—for example, 200 mg. daily for adults in the M.R.C. (1952) trials. In all cases the level of isoniazid was found to be in the therapeutic range. The plasma levels of isoniazid ranged from 0.3 to 0.9 mg. per 100 ml. in the controls, with an average of 0.5 mg., and from 0.25 to 0.61 mg. in the diabetics, with an average of 0.41 mg.

TABLE I.—*Dosage and Plasma Levels of Isoniazid*

Case No.	Sex and Age	Weight lb.	Weight kg.	Total Oral Daily Dose of Isoniazid	Plasma Concentrations of Isoniazid 1½ hrs. After Half the Total Daily Dose: Day Before Test B	Test B	Test C
Controls:					mg./100 ml.	mg./100 ml.	mg./100 ml.
1	M 25	153	69·4	350 mg.	0·8	0·4	0·7
2	M 30	187	84·8	426 ,,	0·3	0·6	0·9
3	M 35	124	56·2	280 ,,	0·3		0·5
4	F 18	118	53·5	270 ,,	0·3	0·4	0·5
5	F 16	134	60·8	300 ,,	0·5	0·45	0·9
6	F 25	109	49·4	250 ,,	0·6	0·3	0·3
Diabetics:							
1	M 39	143	64·9	325 mg.	0·36	0·34	0·35
2	M 38	136½	61·9	310 ,,	0·47	0·53	0·50
3	M 25	157½	71·4	360 ,,	0·41	0·32	0·40
4	F 49	175	79·4	400 ,,	0·5	0·42	0·61
5	F 25	137	62·1	310 ,,	0·4	0·25	0·39
6	F 36	134	60·8	300 ,,	0·33	0·31	0·48

Reducing Activity of Isoniazid.—The reducing capacity of isoniazid in terms of milligrams of sugar was estimated in order to demonstrate that the rise in blood-sugar levels after isoniazid could not be accounted for by isoniazid alone. Isoniazid added to blood in a concentration of 0.5 mg. per 100 ml. had no effect on the sugar estimation by the Folin–Wu method. It was also found that 100 mg. of isoniazid per 100 ml. had a reducing power equivalent to 37.3 mg. of glucose per 100 ml. These findings show that a rise in blood-sugar levels in these experiments cannot be ascribed to isoniazid.

Blood-sugar Curves in Controls.—The blood-sugar values for the six controls are set out in Table II, and those for the six diabetics in Table III. The average curve for the controls (Fig. 1) and for the diabetics (Fig. 2) adequately represent the pattern of any individual case. A study of the results (Table II) shows that isoniazid (1) causes a temporary rise in the fasting blood-sugar level (Table IV), (2) delays the peak of the curve, since the level at one hour is higher than at half an hour, and (3) delays the fall of the curve—the return to the fasting level not occurring, on average, until three hours.

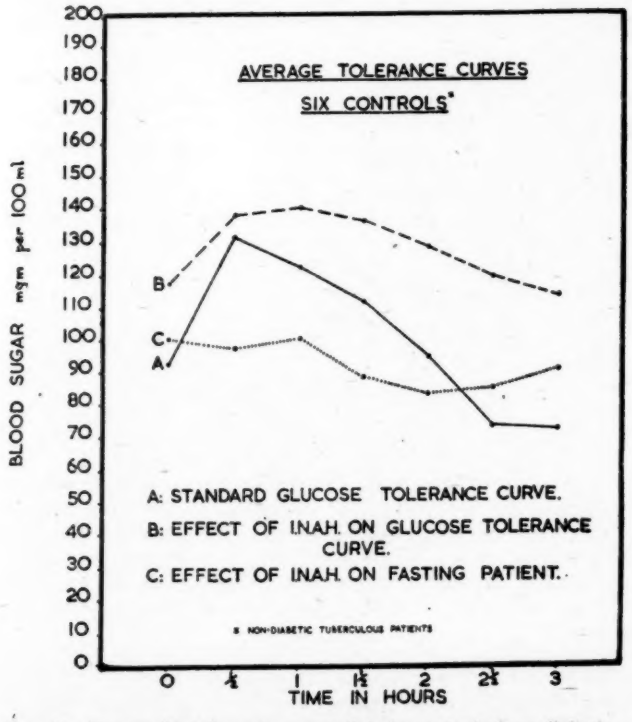
AVERAGE TOLERANCE CURVES
SIX CONTROLS*
BLOOD SUGAR mgm per 100 ml
TIME IN HOURS
A: STANDARD GLUCOSE TOLERANCE CURVE.
B: EFFECT OF INAH. ON GLUCOSE TOLERANCE CURVE.
C: EFFECT OF INAH. ON FASTING PATIENT.
* NON-DIABETIC TUBERCULOUS PATIENTS

FIG. 1.—Composite tolerance curves for six controls (non-diabetic tuberculous patients), showing tests A, B, and C.

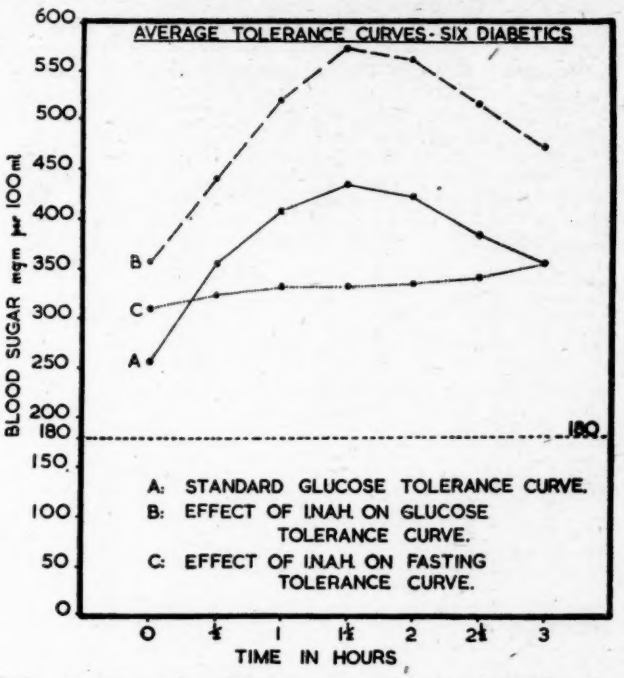
AVERAGE TOLERANCE CURVES - SIX DIABETICS
BLOOD SUGAR mgm per 100 ml
TIME IN HOURS
A: STANDARD GLUCOSE TOLERANCE CURVE.
B: EFFECT OF INAH. ON GLUCOSE TOLERANCE CURVE.
C: EFFECT OF INAH. ON FASTING TOLERANCE CURVE.

FIG. 2.—Composite tolerance curves for six diabetic cases, showing tests A, B, and C.

The rise in the fasting level in each instance after three days' isoniazid (test B) is a temporary one, as the level is reduced again after six days' isoniazid (test C), though not to the level before isoniazid (test A), except in one case.

Blood-sugar Curves in the Diabetics.—The curves in the diabetics show much the same pattern, though in an exaggerated form. All but one (Case 4) of the six diabetic cases were severe, as shown by the standard glucose-tolerance curve. After three days' isoniazid (test B) the fasting levels and all other levels up to three hours are significantly higher. After six days' isoniazid (test C) the fasting levels have dropped a little as in the case of the controls, but not so significantly (Table IV). The levels continue to rise slowly up to three hours.

TABLE II.—*Blood-sugar Values for Six Controls, Showing Tests A, B, and C*

Case No.	Venous Blood Sugars (mg. per 100 ml.) Time in Hours: Fasting	½	1	1½	2	2½	3
Test A:							
1	90	109	132	124	109	80	60
2	85	145	112	104	85	70	60
3	104	160	158	120	112	75	90
4	90	117	132	109	85	75	75
5	100	124	90	—	—	—	—
6	85	132	109	100	80	65	75
Average ..	92	131	122	111	94	73	72
Test B:							
1	120	189	179	141	120	117	117
2	130	137	141	141	141	112	112
3	125	141	137	141	137	137	125
4	117	141	137	132	124	129	106
5	106	106	141	141	138	116	116
6	104	112	105	117	110	105	104
Average ..	117	138	140	136	128	119	113
Test C:							
1	97	100	124	77	64	58	74
2	95	100	109	100	78	81	95
3	104	92	85	82	81	92	91
4	91	91	88	86	88	74	83
5	117	127	104	97	109	109	114
6	97	74	88	88	78	93	86
Average ..	100	97	100	88	83	84·5	90·5

TABLE III.—*Blood-sugar Values for Six Diabetics, Showing Tests A, B, and C*

Case No.	Venous Blood Sugars (mg. per 100 ml.) Time in Hours						
	Fasting	½	1	1½	2	2½	3
Test A:							
1	312	418	456	510	470	462	418
2	173	271	321	385	447	424	374
3	224	288	349	394	371	357	341
4	193	297	336	249	208	186	148
5	284	422	520	584	528	454	432
6	341	432	460	482	512	422	412
Average ..	254·5	355	407	434	423	384	354
Test B:							
1 ..	435	540	600	720	720	590	600
2 ..	434	474	540	668	684	700	656
3	210	321	415	415	425	370	360
4	256	370	492	370	346	287	236
5	422	470	514	656	676	600	506
6	382	470	540	610	518	530	478
Average ..	356·5	441	517	573	561·5	513	473
Test C:							
1	362	432	432	432	377	432	470
2	387	402	471	437	471	483	550
3	190	223	221	246	284	269	249
4	187	170	165	162	142	135	110
5	320	340	305	330	358	363	381
6	395	370	384	370	366	335	362
Average ..	307	323	330	330	333	336	354

TABLE IV.—*Variations in Fasting Blood-levels After 5 mg. of Isoniazid per kg. per Day*

	Fasting Blood-sugar Levels (mg. per 100 ml.)	
	Controls	Diabetics
Before isoniazid (test A) ..	92±8	255±21·5
After three days' isoniazid (test B)	117±11	357±98
After six days' isoniazid (test C) ..	100±8·5	307±95

Variations in Fasting Blood-sugar Levels.—The variations in the fasting blood-sugar levels after isoniazid are shown in Table IV. There was a significant rise in both controls and diabetics after three days' isoniazid and a significant fall again after six days' isoniazid, though not to the level obtained before isoniazid. The figures suggest that the rise is a temporary one, but further work is required to elucidate this point.

Urine Findings.—Urine examinations were carried out on each patient in tests A, B, and C. Case 1 of the controls showed unsuspected renal glycosuria. Specimens 3–7 in test A showed the presence of reducing substances (1 plus Benedict), and these were shown to be glucose by the osazone test and sugar chromatograms. After three days' isoniazid (test B) this patient had a 2-plus Benedict's test in specimens 2–7. A trace of reducing substance was found in several of the urines from the other controls when on isoniazid dosage. The quantity was enough to turn the Benedict's solution green in these cases. The reducing substance was not glucose. The finding of traces of reducing substances in the urine during isoniazid therapy is therefore by no means constant. Urine examination in the diabetics showed that all six patients had large amounts of glucose in the urine as expected. There was moderate glycosuria in test A, increased glycosuria in test B, and a diminution of glycosuria in test C. Glucosazone tests were positive, and sugar chromatographic studies revealed that the sugar was glucose in all cases.

Behaviour of Isoniazid in Solution.—Isoniazid can be readily shown to reduce Benedict's solution. Ten isoniazid solutions of concentrations ranging from 12 to 120 mg. per 100 ml. showed a very faint reduction at 24 mg., increasing to a typical trace reaction at 120 mg. If we assume that a patient is given 300 mg. of isoniazid a day, of which 60% is excreted during that day, and that the volume of urine excreted during this period is 1,500 ml., the resulting concentration of isoniazid is 12 mg. per 100 ml. From these considerations, concentrated specimens of urine, taken when the drug is being most rapidly excreted, may give some reduction due to isoniazid itself.

Sugar Chromatographic Studies.—A one-dimensional sugar-chromatogram showed that four runs made with pure sugar solutions, and four made with urine from tuberculous patients without diabetes but on isoniazid (controls), all showed no sugar or negligible traces of sugar. In four others done with urine from diabetic patients on isoniazid the urines showed a strong excretion of glucose only.

Summary of Results.—The findings are summarized in Tables IV and V, and show that after the administration of isoniazid (1) the fasting blood-sugar level is elevated; (2) the blood-sugar curve rises more slowly; and (3) the oral glucose-tolerance tests are slower to return to normal levels. The finding of trace reductions in urines from patients on isoniazid depends on the concentration of the urine and the rate of excretion of isoniazid at the time. It is thus irregular. A minimum concentration of 24 mg. of isoniazid per 100 ml. is necessary to give a reduction.

TABLE V.—*Changes in Oral Glucose Tolerance Test After Isoniazid*

		Blood Sugar as % of Fasting Level at			
		½ hr.	1 hr.	2 hrs.	3 hrs. after Oral Glucose
Before isoniazid	Controls	142%	132%	102%	78%
	Diabetics	139%	160%	166%	139%
After three days isoniazid	Controls	118%	120%	110%	97%
	Diabetics	123%	145%	158%	133%

Discussion

The results indicate that the administration of isoniazid produces a temporary elevation of blood-sugar level and makes both the rise and fall of an oral glucose-tolerance test slower. As we have shown, isoniazid itself, although a reducing agent, is not responsible for the rise in blood-sugar levels. Thus a disturbance in carbohydrate metabolism may be inferred. We do not know how isoniazid impairs carbohydrate tolerance, but it may be relevant that the glucose-tolerance test in vitamin-B deficiency is similarly abnormal. Lepkovsky, Wood, and Evans (1930) reported that rats approaching their final breakdown from beriberi show a poorer glucose tolerance than their controls, which have been maintained on an identical diet but including adequate vitamin B. Lepkovsky *et al.* (1930), Bueding, Stein, and Wortis (1941), and Elsom, Lukens, Montgomery, and Jonas (1940) have all shown that in the advanced stages of aneurin deficiency glucose-tolerance curves are usually high and prolonged, indicating some impairment of the ability to utilize glucose. These abnormalities do not arise from impaired absorption, since Pachman (1941) showed that they also occur after the intravenous injection of glucose.

In the non-diabetic control patients a mean rise of blood sugar of about 20 mg. per 100 ml. over the three hours of the glucose-tolerance curve is observed, and the rise in blood-sugar levels in the diabetics was spectacular. Additional significance attaches to these findings in the treatment of tuberculous diabetics. With impaired carbohydrate tolerance insulin requirements may be increased. We have formed a clinical impression, over a short-term period on a limited number of cases, that diabetics on isoniazid are more difficult to control. The following two cases illustrate this.

Case 1

The patient, a woman aged 32, was a known diabetic of 14 years' duration. She developed a right pleural effusion in 1944 which resolved uneventfully after three months'

hospital treatment. In February, 1952, pulmonary tuberculosis was diagnosed following a two-months history of cough, sputum, and loss of weight. She was admitted to the diabetic unit at Romsley Hill Sanatorium on March 28. Her general condition was good, she was afebrile, her E.S.R. was 70 mm. in one hour (Westergren method), her sputum was tubercle-positive, and her chest *x*-ray film showed acute disease confined to the right upper lobe with cavitation in the right upper zone.

Her diabetes before admission had been treated with unrestricted diet and soluble insulin (S.I.) before each meal (36 units t.d.s.). Blood sugars ranged between 172 and 354 mg. per 100 ml. and glycosuria was persistent. She was stabilized on a 2,500-calorie diet and 40 units of S.I. together with 30 units of protamine zinc insulin (P.Z.I.) in the mornings, and 30 units of S.I. in the evenings. Her tuberculosis was treated with rest in bed and a three-months course of isoniazid (200 mg. daily) from April 15 to July 15 with considerable clinical and radiological improvement. Symptoms subsided, she gained 20 lb. (9.1 kg.) in weight, the E.S.R. dropped to 16 mm. in one hour, and her chest *x*-ray film showed considerable clearing of the disease in the right upper lobe, but there was residual cavitation for which surgery will be required. Her insulin dosage had to be raised to 44 units of S.I. and 40 of P.Z.I. in the mornings and 30 units of S.I. in the evenings in order to maintain satisfactory control of her diabetes during the period of isoniazid administration. Three weeks after isoniazid was discontinued she had her first insulin reaction and there was less glycosuria throughout the day. She developed a second insulin reaction two weeks later, and the dosage had to be reduced to 34 units of S.I. and 40 units of P.Z.I. in the mornings and 30 units of S.I. in the evenings. Control of the diabetes was more difficult to achieve during the period of isoniazid administration, and insulin dosage had to be raised. Three weeks after isoniazid was discontinued control of the diabetes was again more satisfactory, and the development of insulin reactions necessitated reduction of the insulin dosage.

Case 2

A woman aged 36 enjoyed good health until February, 1950, when diabetes was diagnosed. This was treated with 15 units of globin insulin daily. Following a haemoptysis on January 8, 1952, pulmonary tuberculosis was diagnosed, and she was admitted to the diabetic unit at Romsley Hill Sanatorium on January 19. Her general condition was fair; she was febrile (temperature 100.6° F.—38.1° C.), her E.S.R. was 46 mm. in one hour (Westergren method), her sputum was tubercle-positive, and her chest *x*-ray film showed extensive bilateral disease with cavitation in both lungs. Her diabetes was poorly controlled and she was stabilized on a mixed dose of 24 units of S.I. and 30 units of P.Z.I. in the mornings and 10 units of S.I. in the evenings, with a 2,500-calorie diet. Her tuberculosis was treated with a three-months' course of streptomycin (1 g. daily) and P.A.S. (20 g. daily) from January 20 to April 20, with moderate clinical and radiological improvement. Symptoms subsided, she became afebrile, the E.S.R. dropped to 15 mm. in one hour, and there was moderate clearing of the disease in both lungs. A three-months course of isoniazid (200 mg. daily) was begun on June 30, and glycosuria became more pronounced and fasting blood sugars were in the region of 200 mg. per 100 ml., so that insulin dosage had to be increased to 32 units of S.I. and 32 units of P.Z.I. in the mornings and 16 units of S.I. in the evenings. So far she has had isoniazid for two months, with some clinical and radiological improvement, but her diabetes has been more difficult to control and her insulin requirements have increased.

Summary

After isoniazid the oral glucose-tolerance test shows raised blood-sugar levels in both diabetic and non-diabetic tuberculous patients.

The insulin requirements of diabetic patients receiving isoniazid may be increased.

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SURGICAL TREATMENT OF INTRACTABLE PHANTOM-LIMB PAIN

BY

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Painful sensations in phantom limbs are common, but they vary in pattern and probably also in their mode of production. Indeed, Riddoch (1941) says that about half the people who undergo major amputations feel pain in their phantoms at some period or other. There are, for instance, the bothersome pains in the stump and phantom associated with tender and irritable stump neuromas, the pains felt in the missing limb at the site of wounding, and other fugitive pre-amputation pains. Many of these pains are transient, and if they do not disappear spontaneously are benefited by simple measures, such as resection of painful neuromas (Bailey and Moersch, 1941; Riddoch, 1941; Henderson and Smyth, 1948), procaine block of the sympathetic chain (Livingston, 1938), or even repeated percussion of stump neuromas (Russell, 1949; Russell and Spalding, 1950). But in a small minority, possibly less than 1% of amputees, the phantom pain is intense and intractable, has features which resemble causalgia, and is not relieved by these measures. It is this type of case that concerns us here.

In 1945 Falconer and Lindsay reported two cases of severe pain in a phantom upper limb which had responded to a high cervical chordotomy, after previous treatments, including resection of neuromas, sympathetic-chain block, and brachial-plexus block, had failed to give relief. Subsequently my experience has increased to 12 patients, all referred to me at the Dunedin Neurosurgical Unit in New Zealand between 1944 and 1949, and all submitted to antero-lateral chordotomy after

simpler measures had proved unsuccessful. These patients have now been followed up for periods of between two and seven years, thereby affording an indication of the permanence of the procedure. Nine patients have been greatly benefited as regards their pain, one is only slightly improved, while in two pain has recurred. Some of those benefited, however, have since developed sequelae of the operation which must be weighed against its benefits.

Phantom Upper Limbs

Six patients had upper-limb phantoms, and their salient clinical features are listed in Table I. Five were amputees, including two Service men of the recent war (Cases 1 and 2),

TABLE I.—*Painful Phantom Upper Limbs Treated by High Cervical Chordotomy*

Case No.	Sex and Age	Reason for Amputation	Site of Amputation	Duration of Pain (Years)	Post-operative Follow-up (Years)	Present State
1	M 29	Gun-shot wound	Upper arm	2	7	Phantom pain relieved
2	M 33	,,	,,	3	7	Phanton pain relieved, but chronic cervical subluxation present
3	M 48	Gangrene following fractures	Elbow	12	5	Phantom pain relieved, but chronic lumbar-disk syndrome present
4	F 44	Gangrene due to vascular lesion	Forearm	6	3	Phantom pain slightly improved
5	M 58	No amputation; brachial-plexus lesion		20, slightly; 1½, severely	2	Phantom pain relieved
6	M 38	Crushing injury	Forearm	1	½	Pain recurred within one month. Later topectomy. Suicide

while the remaining patient had sustained a complete tear of the brachial plexus. Each described his pain as of burning or aching quality, located mainly in the thumb, fingers, and occasionally also the wrist of the missing hand, and associated with feelings of involuntary clenching or squirming movements of the fingers. In Cases 1, 2, and 6 pain had been present right from the time of amputation, while in Cases 3 and 4 its appearance had been delayed for six and four years respectively. The patient with the brachial-plexus tear had experienced mild pain for over 20 years, dating back to the time of injury, but pain had been distressing only for the last one and a half years. None of the amputees had any serious pain in his stump, but one suffered from frequent jactitations of the stump (Case 4).

Each patient had previously undergone other operative procedures with little or no benefit. All the amputees had had their stumps trimmed and their neuromas resected. Cases 4 and 5 had undergone some form of sympathectomy. A diagnostic sympathetic block was performed in the remaining four patients, but with beneficial effect in only two of them. In Case 3, in which the block did seem to afford relief, I subsequently carried out a Smithwick sympathectomy, but the patient's pain recurred within a month. Each patient was also tested by a brachial-plexus block, and in four there was no relief of pain. Case 4, in which the test seemed to benefit, subsequently underwent a posterior rhizotomy of C 4–T 1 inclusive, but the pain returned within three weeks. The two patients seen most recently (Cases 5 and 6) were also treated by repeated percussion of neuromas, but with only partial and fleeting benefit.

All six patients were then submitted to a high cervical chordotomy performed under local analgesia, so that the sensory loss resulting from any incision in the cord could be checked immediately. In each patient the antero-lateral column of the cord on the side opposite to the stump was incised between the C 1 and C 2 roots. The incision was made in stages, the initial cuts usually numbing only the lower limb and the lower part of the trunk. Thereafter the incision was deepened and extended until pain was relieved in the phantom. We found this did not occur until the level of analgesia had risen to include the stump. By this time we usually found that the antero-lateral column had been incised to a depth of 5 to 6 mm. at a point immediately in front of the ligamentum denticulatum, and that the

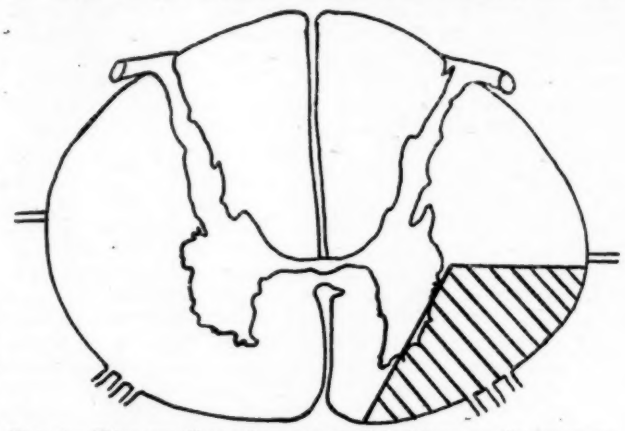

FIG. 1.—Diagram illustrating extent of incision usually necessary in high cervical chordotomy.

incision had been carried forwards to emerge on the surface about 3 mm. anterior to the line of the anterior nerve roots (Fig. 1). Such a depth of incision correlates well with Walker's (1940) observations on the position and extent of the pain and temperature fibres in the cervical cord (Fig. 2).

When tested during the convalescent period each patient had a complete loss of pain and temperature sensibility below the C 4 and C 5 segmental levels. Touch was spared, and there was usually a contralateral Horner's syndrome. The phantom itself was still present, but was now painless. Often the patient remarked that he felt he had regained some control over the movements of the phantom digits. As regards the later results, continued relief of pain has been noted in four patients, but in Cases 4 and 6 there has been some return of pain. Case 4, however, is no longer so disturbed as formerly. In Case 6 severe phantom pain returned within three to four months of operation, and subsequently was eased only slightly by a topectomy; ultimately this patient took his own life.

However, the four patients whose phantom pains were permanently relieved have each developed other symptoms, although on balance each is better than he was before operation. The first patient remained free of complaints for six years, but wrote recently saying that his stump is now "very sensitive and objects strongly to any pressure," although he has not yet mentioned this to his doctor. When I personally examined him five years after operation the loss of pain sensibility was still complete, whereas in the re-

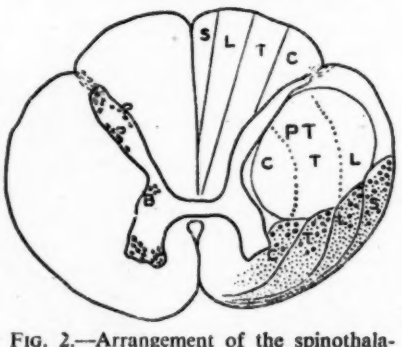

FIG. 2.—Arrangement of the spinothalamic and other tracts in the lower cervical region of the spinal cord, according to A. Earl Walker (1940). The heavy dots represent fibres concerned with temperature; medium dots, fibres mediating pain; and fine dots, fibres carrying touch and pressure impulses. Note the lamination of the tracts. S represents fibres conveying impulses from the sacral segments, L lumbar, T thoracic, and C cervical.

maining three patients some return of pain sensibility in the leg and trunk was noted after a year, and continued or rapidly repetitive painful stimuli applied to these parts gave rise to irritative and burning sensations. Two patients developed even more serious complications. One of them, about seven months after operation, returned to a clerical occupation which involved much flexion of his neck, and shortly afterwards developed a chronic subluxation of C 2 vertebra on C 3, and of C 3 vertebra on C 4. The other, several months later, developed a chronic fourth-lumbar-disk syndrome which did not respond to prolonged conservative treatment, and in the end was treated by operation with some improvement. It is possible that this last complication was provoked by a lumbar puncture.

Phantom Lower Limbs

Six of my patients had lower-limb phantoms, and their particulars are set out in Table II. All were amputees, three of them being Service men (Case 7, Norwegian seaman; Case 9, 1939–45 war; Case 12, 1914–18 war). Each described his pain as either burning or aching, and situated in the toes and forefoot of the missing limb, and perhaps also in the heel and ankle. In three the phantom digits were either squirming or rigidly flexed, but in the others the motor state of the missing limbs was not recorded. Two of the patients had tender hyperaesthetic stumps, and three showed marked jactitation of the stump. In four patients the pain had appeared immediately after a surgical operation, which in two was the primary amputation (Cases 8 and 11), in the third was a reamputation occasioned by failure of the first amputation to heal (Case 7), and in the fourth was a resection of stump neuromas (Case 9). In Cases 10 and 12 pain was delayed in appearance for two months and one month respectively.

TABLE II.—*Painful Phantom Lower Limbs Treated by High Thoracic Chordotomy*

Case No.	Sex and Age	Reason for Amputation	Site of Amputation	Duration of Pain (Years)	Post-operative Follow-up (Years)	Present State
7	M 36	Infected G.S.W.	Mid-thigh	3½	3	Phantom pain relieved
8	M 56	Infected compound fracture	,,	7	5	,,
9	M 29	,, ,,	,,	4	3	Pain relieved, but paraesthesiae in foot
10	F 33	Suppurative arthritis of knee	Lower thigh	3	3	Phantom pain relieved
11	M 68	Infected compound fracture	Mid-leg	8	2	Pain recurred within two months
12	M 61	Infected G.S.W.	Upper thigh	28, intermittently; 2, severely	2	Phantom pain relieved

Each patient had previously undergone a resection of neuromas, and Case 7 had even had his limb reamputated three times at successively higher levels. Only Case 12 was benefited by these procedures, and in this particular patient resection of neuromas had been performed three times in the course of 28 years, on each occasion conferring benefit for from three to ten years. The neuromas were no longer accessible and percussion treatment failed to benefit him. Each patient was also treated by a lumbar sympathetic block and by amylocaine hydrochloride spinal analgesia. In each instance the sympathetic block subjectively warmed the phantom, but in only Case 10 did it relieve the pain, and then only temporarily. In Cases 8, 10, and 11 amylocaine was reported as easing pain, but in the others it had no effect.

All six patients were submitted to a high thoracic chordotomy performed under general anaesthesia at the level of the T 2 and T 3 vertebra. In each patient the antero-lateral column on the side opposite the stump was incised to a depth of 3 to 4 mm. immediately in front of the ligamentum denticulatum, and the incision carried forwards to emerge on the surface 2 to 3 mm. in front of the line of anterior nerve roots. In my experience there is no need to perform thoracic chordotomy under local analgesia, as such an incision constantly produces a satisfactory degree and extent of analgesia.

Following operation, in each patient loss of pain and temperature sensibility was apparent below the T 5 to T 7 segmental levels on the side of the stump, while the sense of pain in the phantom disappeared, although, as with the upper limbs, the phantom itself remained. In Case 11, however, pain returned within two months, while in Case 3 a continuous feeling of pins-and-needles appeared after six months in the phantom foot. In the remaining four patients the relief of pain has continued for from two to five years. One of these (Case 7) when last heard of had epigastric pain suggestive of a peptic ulcer; this presumably was unrelated to chordotomy. Case 10 had undergone an amputation of her second leg, also for chronic suppurative arthritis, but 18 months later had not developed pain in the new phantom.

Discussion

Thus antero-lateral chordotomy would appear to offer prolonged, if not permanent, relief from severe pain in a high proportion of phantom limbs, both upper and lower, but not in all. It is interesting to note how it compares with other methods of treatment, and what light it throws on the mechanisms by which phantom phenomena are produced.

Phantom-limb pain of the type considered in this report is rare, occurring in possibly less than 1% of cases. Ewalt, Randall, and Morris (1947) found only eight such cases in a group of 2,284 American Service men, and Henderson and Smyth (1948) only two or three among some 300 amputees in a prisoner-of-war camp. My own experience is probably similar. I cannot tell what proportion of civilian amputees were represented by my patients, but three of them were New Zealand Service men injured in the recent war, and, including these, the New Zealand War Pensions Office has knowledge of only four or five such cases occurring in a total of 496 surviving amputees (D. Macdonald Wilson, 1951, personal communication).

The rarity of the condition and the fact that the sufferers often show evidence of a disturbed personality have led some clinicians to regard the pain as largely a psychological disturbance (Bailey and Moersch, 1941; Ewalt, Randall, and Morris, 1947; Henderson and Smyth, 1948). Guillaume, Froideveaux, and Mazars (1947) and Kolb (1950) have even described cases which were benefited by psychotherapy, while Pisetsky (1946) reported a case cured by electric convulsion therapy. Certainly some of my patients were greatly demoralized by pain, and were perhaps unstable individuals, but so are many sufferers from other organic painful conditions, such as trigeminal neuralgia. Most of my patients had previously been seen by psychiatric colleagues, who reported that they could not find any significant psychogenic features, neither could they relieve these patients by psychotherapy. I find it difficult to believe that in my hands antero-lateral chordotomy acted as a psychotherapeutic procedure, when previous operative procedures on the stump had failed to give relief. Instead, I am impressed by the fact that these patients all described their pain in much the same terms, locating the pain mainly in the missing digits and associating it with clenching or squirming of those digits. As their symptoms thus conform to a fairly distinctive pattern, and as there was no possibility of collusion between individual patients, I feel that such painful phantom-limb syndromes must be regarded as organically determined.

Comparison of Various Therapeutic Procedures

It is generally agreed that pain of the severity and intractability shown by my patients is not relieved by any destructive procedure which involves the primary sensory

neurone, such as reamputation of the limb, resection of neuromas, section of nerve trunks or plexuses, or posterior rhizotomy (Leriche, 1939; Riddoch, 1941; White, 1950); neither is it relieved by sympathectomy (White, 1950). My own experiences bear out this view. However, this type of pain is often relieved by such procedures as percussion of stump neuromas, antero-lateral chordotomy, posterior chordotomy, ablation of the post-central gyrus, and, finally, leucotomy, but the relief afforded is not always of the same quality.

Repeated Percussion of Stump Neuromas

Repeated percussion of stump neuromas either with a mallet or with a vibrator is the basis of a simple but often effective treatment introduced by Russell (1949). This procedure generally gives relief from pain for only a few hours at a time, so that repeated and self-administered treatments are necessary, the phantom persisting during these periods of relief. This treatment seems to be most effective for cases with tender neuromas of the type that would be eased by nerve-blocks, but occasionally it will numb the pain of phantom lower limbs even when the pain has not been influenced by deep spinal analgesia (Russell, 1952, personal communication). The treatment, however, is not always effective, and Russell and Spalding (1950) mention that in one group of 18 cases there were eight failures. As most of my cases were operated on before the advent of Russell's papers, I tried his method in only three patients: in Cases 5 and 12 it was unsuccessful, possibly because the neuromas were inaccessible, and in Case 6 it produced some relaxation of pain and posture in the clenched phantom hand, even though a plexus block had been completely ineffective, but the degree of relief it afforded did not satisfy the patient.

The mechanism of pain relief underlying these observations is not certain. Russell felt that by maintaining the neuromas in a "chronically concussed state" he rendered them insensitive, while the repeated trauma caused the nerve endings to degenerate gradually and be replaced by fibrous tissue. This explanation is possibly faulty, for more certain ways of cutting off abnormal impulses arising in neuromas, such as procaine blocks or even section of the nerve, consistently fail to give relief in the type of case under consideration. Rather, I think, the explanation lies in the fact that by traumatizing the neuroma a barrage of afferent impulses is sent up to the spinal cord, as is postulated in the hypothesis which I shall later develop. Bartlet (1951) has already put forward this explanation, which possibly also accounts for the observations of Bailey and Moersch (1941) that slight pressure on the nerve trunk above the amputation may cause the phantom to disappear, whereas section of the nerve does not.

Antero-lateral Chordotomy

Although Bailey and Moersch (1941), de Guitérrez-Mahoney (1944), and Coleman (1946) were unsuccessful with this method, Riddoch (1941) and White (1950) had experiences similar to mine, while Bromley (1930) reported a successful outcome in a painful phantom of the upper limb which was treated by high cervical chordotomy. The general finding has been that following this operation the pain in the phantom disappears, although the phantom itself persists. This observation, taken in conjunction with the observation that posterior rhizotomy has no effect on such pain, suggests that in the type of case we are considering the structures responsible for the pain are the secondary sensory neurones which have their cell bodies in the substantia gelatinosa of Rolando. In the very few cases in which the operation fails, neurones at still higher levels in the pain-pathways of the central nervous system are presumably perpetuating the pain.

Posterior Chordotomy

Pool (1946) and also Browder and Gallagher (1946, 1948), working independently, investigated the effect of section of the posterior column of the spinal cord. Their hypothesis was that, if the proprioceptive pathways from the whole limb were severed, the cramped posture of the phantom limb might be relieved, and consequently the pain in it, and even the phantom itself might disappear. Pool operated on three cases, all phantoms of the upper limb, dividing the lateral part of the posterior column at the level of the fifth cervical lamina. In at least one patient, operated on under local analgesia, he found that pain was not relieved until the incision had been carried laterally across the line of the posterior nerve roots, and so into the substantia gelatinosa of Rolando. Post-operatively all three patients seemed benefited, the phantom hand being free of pain, but still retaining its sense of position. In each patient diminished sensibility to pinprick associated with an exaggerated response to temperature was observed over the upper thoracic segments. Possibly the explanation of these sensory changes in both the thorax and the phantom lay in the involvement of the secondary sensory neurones of the substantia gelatinosa. The benefit seen in Pool's cases, however, was not permanent (Pool, 1952, personal communication).

Browder and Gallagher operated on six cases, comprising four lower-limb phantoms and two upper-limb phantoms. For the lower-limb cases they divided the whole of the dorsal column on the appropriate side at the mid-thoracic level. For the upper limb they operated at the C 2 level, sectioning the lateral two-thirds of the dorsal column without disturbing gait or stance. After dorsal chordotomy, complete loss of the phantom foot as well as the cramp-like pain occurred in three patients; in the other pain was relieved, but the phantom persisted. In none of these four patients was there any disturbance of motor power in the stump or of touch, although vibration sensibility in the stump was diminished in three. The results in the two cases of phantom upper limb were difficult to evaluate, and neither case could really be regarded as successful. Browder (1952, personal communication), however, said that the benefit observed in the lower-limb cases has been permanent.

The rationale of these operations is difficult to understand, for the fibres in the posterior column are the proximal axons of cells in the dorsal root ganglia, and yet posterior rhizotomy which severs the same axons but at another site does not relieve pain.

Ablation of the Post-central Gyrus

In 1944 de Guitérrez-Mahoney reported having successfully relieved pain in a phantom upper limb by excision of the appropriate area of the post-central gyrus of the opposite cerebral hemisphere. Since then other surgeons, also operating under local analgesia, have confirmed that stimulation of the appropriate area with an electrical current prior to excision will intensify the pain, while resection of the area will abolish the awareness of the phantom in addition to the pain. There is, however, some doubt about the permanence of pain-relief after this operation. Thus Echols and Colclough (1947) and Stone (1950), who, like de Guitérrez-Mahoney in his first paper, reported their experiences shortly after operation, claimed good results, but Horrax (1946, 1948) and Sunderland and Kelly (1948) stated that in their cases pain has usually returned within a few weeks or months. Evidently this has been de Guitérrez-Mahoney's own experience, for in 1948 he stated that in three out of his four personal cases there had been some return of pain after several weeks.

The fact that stimulation of the post-central gyrus intensifies the pain while excision of the gyrus destroys the phantom as well as the pain suggests that the sensations connected with the phantom enter into consciousness, at least partly, in this area. In discussing his long-term findings, de Guitérrez-Mahoney drew attention to the second sensory cortical area described by Adrian (1940), by Woolsey and Fairman (1946), and by Penfield and Rasmussen (1950), which is situated along the upper bank of the Sylvian fissure in the parietal region, and which receives sensory impulses from both sides of the body. It would seem possible that the return of pain some time after post-central gyrectomy may be due to increased functioning of this second sensory area.

Frontal Lobotomy

Several surgeons, notably Van Wagenen (1944), Watts and Freeman (1948), and Waugh, Cameron, Howarth, and Matas (1949), have reported successful results in painful phantoms after prefrontal leucotomy, while Le Beau (1950) has observed benefit following topectomy. The relief produced by these procedures is presumably similar to that observed following these same operations for pain due to malignant disease and other organic pain-states, in that the pain persists but no longer worries the patient as formerly. Some degree of emotional blunting is probably inseparable from a beneficial response. Therefore such operations should not be tried or contemplated for painful phantom limbs until other measures, such as percussion of neuromas and antero-lateral chordotomy, have been tried and have failed.

Mechanism of Pain-production

Weir Mitchell (1872), in his classical paper, postulated that the phenomena of phantom limbs were due to an "ascending neuritis" spreading up from the severed ends of peripheral nerves. No one, however, has ever demonstrated the histological changes of inflammation within the nerves, but variations of the theory substituting local irritation of nerve fibres within the neuromas or at the cut ends of nerves can readily be advanced to explain why some painful phantoms, principally those of milder degree, are eased by resection of stump neuromas. The "peripheral" theory, however, will not explain why phantom phenomena persist when the peripheral nerve is blocked or sectioned, nor will it explain the method of pain relief in the intractable cases which have here been considered. Hence some have argued that the mechanism must be a central one, situated in the cortex (Henderson and Smyth, 1948).

Certainly, as I have already mentioned, the evidence afforded by stimulation of the post-central gyrus in conscious patients and the effects of its excision suggests that in some way phantom sensations enter into consciousness in this cortical area. But these sensations may still arise from the activity of nerve cells intermediate between the cortex and the peripheral neurone. In an earlier paper (Falconer and Lindsay, 1945) it was pointed out that, in cases with intractable pain, antero-lateral chordotomy renders a phantom painless, whereas posterior rhizotomy does not, and consequently that the neurones presumably responsible for the pain are the cells of the substantia gelatinosa of Rolando. I would like to develop this hypothesis further in the light of more recent evidence, both theoretical and experimental.

When a peripheral nerve is sectioned the stream of afferent impulses, which used to pass up it continuously to the spinal cord, either ceases completely or is grossly diminished and distorted. The observations of Weddell, Sinclair, and Feindel (1948) on the anatomical basis underlying pain in painful scars are germane in this connexion. They compared the distribution of nerve fibres in painful and painless scars with that in normal skin, and found that in painful scars the nerve endings were arranged in isolated fashion, and not interwoven as in normal skin and in sensitive but painless scars. They argued that the pattern of sensory impulses relayed to the spinal cord from these painful areas was probably an incomplete one, and that it was this distortion of the pattern rather than the diminution in the total number of impulses which resulted in the sensorium discerning the diffuse and aching pain that is characteristic of hyperpathia. Possibly the same principles can be used to explain painful phantoms, for, because of the section of several peripheral nerves inevitable in an amputation, a distorted as well as a diminished pattern of impulses must reach the cells of the substantia gelatinosa, and the harmonics of this pattern may be such that unusual painful impulses are evoked. If the stump neuromas are then percussed, a barrage of afferent impulses is conveyed up the hitherto relatively silent peripheral nerve, and perhaps restores both the pattern and the intensity of the afferent impulses to more normal limits.

Eccles and McIntyre (1951) have described experiments which may help to explain the actual changes that may occur in the synapses around the cells of the substantia gelatinosa. In their experiments in cats they sectioned several posterior nerve roots serving one hind limb, dividing the roots just distal to their ganglia, and then allowed the animals to recover. Several weeks later they stimulated these same posterior roots singly at sites proximal to the ganglia, and observed the changes which had taken place in the monosynaptic (two-neurone) reflex arcs that form the basis of the ankle-jerk and other simple myotatic stretch-reflexes. To control their work they stimulated the nerve roots adjacent to the operated area, as well as the nerve roots on the unoperated side. They recorded several important findings. First, the operative section greatly impaired the reflex effectiveness of stimulating the dorsal root. For instance, a single momentary electrical stimulus applied to the root would no longer evoke a contraction in the muscle. Secondly, if the reflex arc was first conditioned by a tetanizing stimulus—for example, 6,000 volleys at 400 volleys a second—the muscle would respond to a single momentary stimulus (single volley) given even several minutes after the tetanizing stimulus had ceased. The influence exerted by this tetanizing stimulus lasted longer on the operated than on the control side, although the muscle response was less on the operated side. Thirdly, they found that if the dorsal root immediately rostral to those operatively divided was stimulated, its reflex effectiveness was greater than that of its companion on the unoperated side. Eccles and McIntyre thought that these observations indicated that usage leads to increased functional efficiency of synapses and disuse to defective function, and also that, when habitual afferent impulses are cut off, stimulation along other pathways may sometimes result in increased potentiation of motor neurones. It seems not unreasonable to apply these observations to the state of the cells of the substantia gelatinosa following an amputation by conceiving that when these cells are cut off from their normal pattern of afferent impulses they may become stimulated by impulses from other pathways. Further, percussion of the stump neuromas may act like a tetanizing stimulus and help to condition the nerve cells to react in a more normal manner.

I therefore postulate that the explanation of severe pain in phantom limbs, of the type here surveyed, is that the cells of the substantia gelatinosa, cut off from their normal-patterned stream of stimuli, discharge spontaneously or react to unusual sources of stimuli, and so provoke pain. This explanation would account for many features of the syndrome, and is in keeping with the neuro-anatomical and neuro-physiological observations just considered.

Summary

Experiences gained in treating 12 patients with intractable phantom-limb pain are recorded, six of whom had involvement of an upper limb and six of a lower limb. Each patient had suffered severe pain for some considerable time, mostly a matter of years, and many of them had previously been treated by such measures as resection of stump neuromas, sympathectomy, or re-amputation without benefit. Each patient was then submitted to an antero-lateral chordotomy at an appropriate level and subsequently a pronounced relief of pain was observed in nine of them, slight benefit in one, and a return of pain in the remaining two.

Pain of the type and severity shown by these patients is rare after amputation. Several other measures, including percussion of stump neuromas, antero-lateral chordotomy, posterior chordotomy, post-central gyrectomy, and leucotomy, may relieve such pain, and their respective merits are discussed.

It is felt that in the type of case described anterolateral chordotomy gives the best results. The mechanism of pain production and its relief by the various treatments is discussed.

Mr. Anthony James and Dr. D. Macdonald Wilson, both of New Zealand, have given me much assistance in following up my patients. I am also grateful to Professor J. C. Eccles and to Dr. T. McLardy for helpful discussions regarding the mechanism of phantom-limb pain.

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The annual report on the medical services of Nigeria for 1950–1 contains an account of a scheme to eradicate mosquitoes at Ilaro in Southern Nigeria. The scheme was based on the suggestions of the Expert Committee on Malaria of the World Health Organization, and the preliminary malaria survey began in 1949. Ilaro has some 12,000 inhabitants and 2,300 houses, and is a typical mixed urban and rural community situated within a geographical zone where hyperendemic malarial conditions exist. *P. falciparum* is the main parasite species but there is also *P. malariae*. *A. gambiae* and *A. funestus* are the main vectors, with *A. funestus* persisting throughout the year, while *A. gambiae* has a pronounced seasonal importance during the rains. Residual spraying began in March, 1950. The insecticide used was the benzene hexachloride wettable powder "P.520," containing 6.5% of the gamma isomer. The spraying of the 2,300 houses, containing over 11,000 rooms, is being repeated every three months and the results are now being assessed by the study of entomological and malariometrical data. According to the report it is still too early to assess the results of this scheme, which must last for three full years before any valid information is obtained. Nevertheless the preliminary results have shown that there has been a spectacular decrease of adults of *A. funestus*. The decrease of malariometrical indices in the local population has been slow, but this was not unexpected in an area previously "saturated" with malaria. The most pronounced reduction of the parasite rate occurred during the last half of 1950 in very young children. There was also a considerable reduction of malaria morbidity recorded at the Ilaro dispensary. The scheme is costing about £3,000 per year, or approximately 5s. per head of the local population.

DETECTION OF TUBERCULOSIS IN GENERAL PRACTICE BY PHOTOFLUOROGRAPHY

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Stradling (1948) has shown that the average apparent diagnostic delay in cases of pulmonary tuberculosis referred to his chest clinic at Hammersmith amounted to six months. Procrastination for two months occurred before the patient sought medical advice. The general practitioner waited an average of four months before he referred the patient to the clinic for special chest investigation. For years Toussaint (1946) and others have stressed that, if we are to find our cases earlier, minor respiratory and other symptoms in people who are not ill must be regarded as indications for a chest *x*-ray examination. Stradling lists the following symptoms or conditions based on Toussaint (1946) as indications for a chest *x*-ray film: cough, haemoptysis, dyspnoea, laryngitis, lassitude, bronchial catarrh, pneumonia, influenza out of season, recurring febrile chills, P.U.O., pleurisy, pleurodynia, or pain in chest, loss of weight, anorexia, anaemia and debility, amenorrhoea (unexplained), ischio-rectal abscess, erythema nodosum, phlyctenular conjunctivitis, contact.

X-ray Film Requirements

It was decided to ascertain the incidence of these symptoms, to which reflex dyspepsia was added, in a general practice of 3,500 in Wandsworth. In the single month of March, 1949, 155 patients of one of us (T. J. L.) complained of or presented with one or more of the above symptoms. Of the 155, 106 attended the surgery with these symptoms for the first time in March, 1949; 30 had previously attended with the same or allied symptoms in January or February, 1949; and 19 had come with the same or allied symptoms in October to December, 1948. All the 155 patients were referred for photofluorography. Had the scheme been in operation before March, 1949, presumably at least 49 of the 155 patients would already have been *x*-rayed. Later, over a period of two years, it was found that, using clinical judgment, about 20 films a month were required for the practice of 3,500. *This is just over five films a month per thousand patients* in the practice. The general practitioner ordering the *x*-ray examination had spent many years in general practice and had also had considerable experience of modern sanatorium treatment. This practice is probably representative of the area, and therefore a provisional estimate of the number of films required to be taken for general practitioners, using the indications previously mentioned, in a chest clinic area with a population of 200,000 would be 1,000 chest *x*-ray films a month, or 12,000 a year. Hunt (1951) stated that "during the last three years" 624 chests had been *x*-rayed—apparently in a practice of about 3,800. This gives an average of about 4.5 films per 1,000 patients a month, which is very similar to our figure of 5 per 1,000 a month.

Trenchard and Grenville-Mathers (1952) have said: "Instead of throwing the diagnostic net of the clinics ever

wider, a halt should be called when a chest clinic serving a population of about 200,000 is seeing up to 6,000 referred cases a year. This is probably as much as even a properly designed and equipped chest clinic can cope with." According to this authority, therefore, even a properly designed and equipped chest clinic could cope with only half the number of examinations which, according to our estimates, are needed. If we take the population covered by a single mass *x*-ray unit to be between half a million and one million, we can see that, by our estimate of a requirement of five examinations per 1,000 patients per month, the general practitioners serving this population will *need* (not necessarily *demand*) 2,500 to 5,000 chest *x*-ray examinations a month, or 30,000 to 60,000 a year. We conclude, therefore, that the present number of mass *x*-ray units available would be adequate to meet the needs of general practitioners for chest examinations only if they did nothing else.

A Scheme for South-west London

Facilities for unlimited miniature chest *x*-ray examinations are now offered to the general practitioners in South-west London, who were sent a letter which stated:

"You may frequently feel the need for access to special investigations without reference to a consultant or hospital. We are able to offer you a scheme whose purpose is to provide a chest *x*-ray for those people who are not ill, but who attend you with minor respiratory and other symptoms, which may indicate the need to exclude relatively early pulmonary tuberculosis.

"I should like to make it clear that the scheme is in no way intended to replace the service offered by a chest clinic. Ill or urgent cases and children under 15 years are quite unsuitable.

"*Diagnostic Value of 35 mm. Chest X-ray.*—It is a very reliable detector of pulmonary tuberculosis. Bronchiectasis, bronchitis, and some early cases of carcinoma of the bronchus may often be passed as 'N.A.D.,' as may cases of dry pleurisy and some heart abnormalities."

The number of doctors now using the scheme is 252 (over 50% of the general practitioners in the area). In designing the scheme it was important to bear in mind the need to save the general practitioner time and trouble, including clerical work. This was achieved by providing instruction slips for the patient, who is required to telephone the mass *x*-ray service and negotiate an appointment to suit his convenience. From the accompanying *x*-ray request form it will be seen that the doctor has only to insert the symptom numbers for which he is referring the patient, and the onset. He gets the result by post the next day.

In 1951 3,720 patients living in the borough of Wandsworth (population 300,000) were *x*-rayed under this scheme. It might be thought that the availability of chest films to general practitioners through the mass *x*-ray unit would cause a falling-off in the numbers attending the chest clinics for the first time, but Table I shows that, on the contrary, the numbers attending the two chest clinics serving the area increased from 1,807 in 1950 (before the mass *x*-ray G.P. scheme was being considerably used) to 2,529 in 1951. Of 476 primary notifications of pulmonary tuberculosis made in Wandsworth in 1951, 7% were discovered through the ordinary mass radiography service, 11% through the mass *x*-ray G.P. scheme, and 82% through other channels.

It is of interest that the primary notifications for Wandsworth of pulmonary tuberculosis rose from 454 in 1950 (before the mass *x*-ray G.P. scheme was being widely used) to 476 in 1951. The total notifications for the London County, on the contrary, had fallen from 5,189 in 1950 to 4,897 in 1951. However, the Wandsworth rise was not the only one to occur in a London borough in this period, and the increase could be explained either as the effect of the new scheme or as a chance fluctuation.

TABLE I.—*Number Attending Chest Clinics for First Time*

Year	Wandsworth Clinic	Balham Clinic	Total
1948	1,147	914	2,061
1949	946	890	1,836
1950	911	896	1,807
1951	1,138	1,391	2,529

Findings

We here describe the findings of the first 3,000 examinations made by the South-west London Mass X-ray Service for general practitioners. Table II shows that, of 3,032 patients *x*-rayed 91 (3%) had radiologically significant lesions, probably tuberculous, requiring investigation. Of these, 60 were classified, after investigation, as active. This gives a rate of 20 active adult-type cases of pulmonary tuberculosis per 1,000 patients examined—that is 1 examinee in 50 had active adult-type pulmonary tuberculosis. (The decision whether to classify a patient as active or inactive was made by chest clinic physicians two months after he had been referred for investigation.)

TABLE II.—*General-practitioner Scheme: Summary of Results*

Disposal	No.	%
Referred to chest physician*	91	3·00
Referred to chest hospital†	18	0·59
Heart or other abnormality	140	4·62
N.A.D.	2,783	91·79
	3,032	100·00

* With lesions probably tuberculous. † With lesions probably non-tuberculous.

Table III shows that the age-and-sex distribution of the 3,032 examinees differed from that of the general population; naturally, few very young and very old patients were submitted. Table IV shows surprisingly that in both sexes the symptoms were more often diagnosed radiologically as tuberculosis in the single than in the married people examined. This higher degree of radiological confirmation of suspicion in single examinees is best seen in the group of single women age 35–44, 15% of whom were found to have radiologically significant lesions, probably tuberculous and requiring investigation.

I HAVE REFERRED PATIENT FOR *X*-RAY COMPLAINING OF

Symptom Nos.	Onset

1. Cough.
2. Reflex dyspepsia.
3. Dyspnoea.
4. Laryngitis.
5. Lassitude.
6. Bronchial catarrh.
7. Influenza, out of season.
8. Recurring febrile chills.
9. P.U.O.
10. Pleurisy, pleurodynia, or pain in chest.
11. Loss of weight.
12. Anorexia.
13. Anaemia and debility.
14. Amenorrhoea
15. Pneumonia.
16. Ischio-rectal abscess.
17. Erythema nodosum.
18. Phlyctenular conjunctivitis.
19. Contact.

Provisional Clinical Diagnosis (if helpful)

REPORT ON FILM

For F. A. NASH
(Medical Director).

TABLE III.—*Age, Sex, Marital Status: Comparison with General Population of London*

	Marital Status	Actual Patients X-rayed	Expected from General Population Distribution*	Excess + (or Deficiency −) of Actual over Expected
Males:				
0–14 years		80	306	−226
15–24 ,,	Single	212	143	+69
	Married†	29	24	+5
25–44 ,,	Single	128	106	+22
	Married	465	377	+88
45+ ,,	Single	53	54	−1
	Married	351	400	−49
All males		1,318	1,410	−92
Females:				
0–14 years		64	293	−229
15–24 ,,	Single	355	152	+203
	Married	122	58	+64
25–44 ,,	Single	155	107	+48
	Married	667	405	+262
45+ ,,	Single	74	121	−47
	Married	277	486	−209
All females		1,714	1,622	+92
Total patients		3,032	3,032	—

* Based on 1951 census, 1% sample tables for London A.C.
† Including widower and divorced.

The higher percentage of tuberculous lesions in single examinees could be due to a number of causes. Single people may, for various reasons, be less likely to attend their doctors for symptoms 1 to 19, listed above, when non-tuberculous or less serious, than married people, so that when they do attend suspicion may be justifiably increased. Conversely, giving the same effect, married people, when off-colour, may be more likely to attend their doctors because they have husbands or wives to send them. The incidence of these symptoms without tuberculous origin could be higher in married people than in single people. Doctors may be "under-referring" single people. Another possible explanation is that there may be more pulmonary tuberculosis among the single than among the married. (Of course, no deductions about this last point are permissible, as our patients are a highly selected group.) So marked is the effect of marital status on the diagnostic yield that its importance often outweighs that of the particular symptom (within the group of symptoms 1 to 20) of which the patient complains.

Does the presence of any particular symptom or symptom-complex give a specially high yield of pulmonary tuberculosis? Some interesting impressions can be gained from scrutiny of Tables V and VI. The reader will be able to

TABLE V.—*Symptoms and Result*

Symptom	Total Sent for *x*-ray	Outcome: Referred to Chest Physician* No.	%	Referred to Chest Hospital† No.	%	Heart and Other Abnormality No.	%	N.A.D. No.	%
Cough	1,727	59	3·4	12	0·7	97	5·6	1,559	90·3
Reflex dyspepsia	124	6	4·8	1	0·8	6	4·8	111	89·6
Dyspnoea	289	9	3·1	2	0·7	23	8·0	255	88·2
Laryngitis	117	5	4·3	—	—	4	3·4	108	92·3
Lassitude	698	20	2·9	4	0·6	20	2·9	654	93·6
Bronchial catarrh	547	9	1·6	5	0·9	54	9·9	479	87·6
Influenza (out of season)	81	2	2·5	—	—	4	4·9	75	92·6
Recurring febrile chills	175	3	1·7	1	0·6	3	1·7	168	96·0
P.U.O.	31	1	3·2	—	—	1	3·2	29	93·6
Pleurisy, pleurodynia, or pain in chest	821	19	2·3	7	0·8	35	4·3	760	92·6
Loss of weight	531	19	3·6	5	0·9	18	3·4	489	92·1
Anorexia	181	8	4·4	—	—	4	2·2	169	93·4
Anaemia and debility	142	6	4·2	—	—	8	5·6	128	90·2
Amenorrhoea	32	—	—	—	—	1	3·1	31	96·9
Pneumonia	51	3	5·9	1	2·0	4	7·8	43	84·3
Ischio-rectal abscess	10	2	20·0	—	—	1	10·0	7	70·0
Erythema nodosum	14	4	28·6	—	—	3	21·4	7	50·0
Phlyctenular conjunctivitis	8	—	—	—	—	—	—	8	100·0
Haemoptysis	26	3	11·5	1	3·9	3	11·5	19	73·1
Contact	262	8	3·0	—	—	6	2·3	248	94·7
No symptoms specified	97	1	1·0	—	—	—	—	96	99·0
Total cases	3,032	91	3·0	18	0·6	140	4·6	2,783	91·8
Average period since onset of symptoms (weeks)‡	14·3	6·8		21·5		15·6		14·4	

* With lesions probably tuberculous.
† With lesions probably non-tuberculous.
‡ Calculated on 961 cases. The numbers of cases on which this average is calculated for the four separate categories of outcome were respectively (from left to right) 18, 2, 23, and 918.

TABLE IV.—*Age, Sex, Marital Status of Patients and Disposal*

	Marital Status	Total Sent for *X*-ray	Referred to Chest Physician* No.	%	Referred to Chest Hospital† No.	%	Heart or Other Abnormality No.	%	N.A.D. No.	%
Males:										
0–14 years		80	1	1·2	—	—	3	3·8	76	95·0
15–24 ,,	Single	212	2	0·9	—	—	9	4·3	201	94·8
	Married	29	—	—	—	—	1	3·4	28	96·6
25–34 ,,	Single	103	8	7·8	2	1·9	2	1·9	91	88·4
	Married	234	8	3·4	—	—	12	5·1	214	91·5
35–44 ,,	Single	25	2	8·0	1	4·0	2	8·0	20	80·0
	Married	231	7	3·0	2	0·9	14	6·1	208	90·0
45+ ,,	Single	53	1	1·9	1	1·9	5	9·4	46	86·8
	Married	351	14	4·0	7	2·0	38	10·8	292	83·2
All males		1,318	43	3·3	13	1·0	86	6·5	1,176	89·2
Females:										
0–14 years		64	4	6·2	—	—	—	—	60	93·8
15–24 ,,	Single	355	13	3·7	—	—	8	2·2	334	94·1
	Married	122	2	1·6	—	—	2	1·6	118	96·8
25–34 ,,	Single	102	5	4·9	—	—	4	3·9	93	91·2
	Married	389	7	1·8	—	—	12	3·1	370	95·1
35–44 ,,	Single	53	8	15·1	—	—	3	5·7	42	79·2
	Married	278	—	—	—	—	9	3·2	269	96·8
45+ ,,	Single	74	3	4·1	1	1·3	7	9·5	63	85·1
	Married	277	6	2·2	4	1·4	9	3·2	258	93·2
All females		1,714	48	2·8	5	0·3	54	3·2	1,607	93·7
Total patients		3,032	91	3·0	18	0·6	140	4·6	2,783	91·8

* With radiologically significant lesions, probably tuberculous.
† With radiologically significant lesions, probably non-tuberculous.

TABLE VI.—*Limited Combinations of Symptoms or Single Symptoms Only*

Symptoms or Combination of Symptoms	Total Cases Referred with Symptoms	Referred to Chest Physician*		Referred to Chest Hospital†		Heart or Other Abnormality		N.A.D.	
		No.	%	No.	%	No.	%	No.	%
1. Cough alone	502	15	3·0	1	0·2	31	6·2	455	90·6
2. Cough, pleurisy, or pain in chest only	157	1	0·6	4	2·6	6	3·8	146	93·0
3. Cough and lassitude only ..	72	6	8·3	—	—	—	—	66	91·7
4. Cough and loss of weight only ..	85	6	7·0	2	2·4	8	9·4	69	81·2
5. Cough, loss of weight, lassitude only ..	47	—	—	—	—	1	2·1	46	97·9
6. Cough, loss of weight, lassitude, anorexia only	8	3	37·5	—	—	—	—	5	62·5
7. Cough, dyspnoea only .	25	2	8·0	—	—	2	8·0	21	84·0
8. Cough, dyspnoea, pain chest only ..	18	—	—	—	—	1	5·6	17	94·4
9. Cough, dyspnoea and loss of weight only ..	10	2	20·0	—	—	1	10·0	7	70·0
10. Cough, laryngitis only ..	29	3	10·3	—	—	1	3·5	25	86·2
11. Cough, bronchial catarrh only ..	86	2	2·3	—	—	5	5·8	79	91·9
12. Pleurisy or pain in chest alone ..	273	5	1·8	2	0·7	10	3·7	256	93·8
13. Reflex dyspepsia alone	20	3	15·0	1	5·0	2	10·0	14	70·0
14. Lassitude alone ..	72	—	—	1	1·4	2	2·8	69	95·8
15. Lassitude, loss of weight only ..	38	—	—	—	—	2	5·3	36	94·7
16. Loss of weight alone ..	62	1	1·6	—	—	—	—	61	98·4
17. Bronchial catarrh alone	84	1	1·2	2	2·4	4	4·8	77	91·6
18. Influenza out of season alone ..	35	1	2·9	—	—	2	5·7	32	91·4
19. Pneumonia alone ..	14	2	14·3	—	—	2	14·3	10	71·4
20. Haemoptysis alone ..	6	—	—	—	—	1	16·7	5	83·3
21. Haemoptysis and cough only	9	1	11·1	—	—	2	22·2	6	66·7
22. Contact alone	122	5	4·1	—	—	2	1·6	115	94·3

* With radiologically significant lesions, probably tuberculous, requiring investigation.

† With radiologically significant lesions, probably non-tuberculous, requiring investigation.

compare these figures with his personal experience so far as his memory or records are quantitative. The presence of symptoms sufficient to send the patient to the doctor, and to get the doctor to use the scheme, gives a yield of 3% of radiologically significant lesions, probably tuberculous, requiring investigation. The hospital clinician may be surprised to see that of 47 people referred with cough, loss of weight, and lassitude none were tuberculous. However, we are dealing with small numbers, and chance fluctuations are correspondingly large. If we combine items 3, 4, and 5 of Table VI we get for "cough with loss of weight and/or lassitude" 12 tuberculous out of 204, or 5.9%. Cough with laryngitis yields 3 tuberculosis suspects out of 29 (10.3%), but cough with "bronchial catarrh" yields only 2 out of 86 examinees (2.3% probably tuberculous). Lassitude alone (72 cases) or lassitude accompanied with loss of weight only (38 cases) did not indicate one case of tuberculosis. Bronchial catarrh alone (84 examinees) or influenza out of season alone 35 (examinees) did not yield any cases of tuberculosis.

The Time Factor

The average period since the onset of symptoms was 14.3 weeks (calculated on 961 cases out of 3,032 in which the doctor had stated the duration on the *x*-ray request form). The duration of symptoms was given for only 18 of the 91 patients who had radiologically significant lesions, probably tuberculous, requiring investigation—and here the average period since onset was 6.8 weeks.

The duration of symptoms according to age and sex was examined in relation to the yield of tuberculosis (referred to chest physician). As might be expected, of 57 people aged 45 and over whose symptoms had lasted more than 13 weeks none had *x*-ray evidence of tuberculosis. Presumably among these were many chronic bronchitics.

It has surprised and pleased us to see the remarkably small extent of the "tuberculous area" in films of cases which were active. *X*-ray evidence of cavitation was absent in 70% of cases. Half (48%) of the cases had only one zone affected; 28% had only two zones affected; 11% had disease in three zones; and only 13% had more extensive disease.

If only one patient in 30 referred has significant pulmonary tuberculosis, does the scheme encourage the profligate and wasteful use of *x*-ray films? Use of the scheme was uneven. Thirteen doctors out of the 183 using it accounted for nearly half the total of patients. So far as cases referred to chest physicians are concerned, there is no suggestion that, on the whole, physicians were using different criteria in selecting patients for radiology. For doctors who used the scheme three times or more but fewer than 25 times the yield of tuberculosis was 2.9%, from 954 patients. Out of the 2,001 patients submitted by doctors who used the scheme 25 or more times in the period reviewed, 2.8% were tuberculous, which is not significantly different from the average percentage of 3.0. Thus, while some practitioners used the scheme more than others, it cannot be claimed that there is any real evidence of diminishing returns, dilution, or overuse in the frequent, as compared with the infrequent, users.

The figures suggest that many doctors made under-use of the scheme, probably because they hesitate to send a patient to hospital for an *x*-ray examination unless there is a fairly high probability that it will show an abnormality. They perhaps hesitate because they have come to feel slightly disconcerted when several patients have been returned to them with negative findings. The general practitioner knows that, from the point of view of his needs, local *x*-ray resources are pitifully inadequate, being already monopolized by the hospital medical departments. We believe that until the general practitioner loses the habits acquired during a lifetime of practice with inadequate diagnostic facilities, tuberculosis will continue to be discovered far later than it should be, with the consequent waste of lives and the costly "medicated survival" of cases which should have been cured if they had been found earlier. With recent advances in treatment, early diagnosis has never before been so important as now, when so much can be done if it is done in time.

The 57 tuberculous cases found by the "frequent users" had 30% cavitation; 51% had one zone; and 19% had two zones affected. The 34 cases referred by doctors who used the scheme less than 25 times had 32% cavitation; 44% had one zone; and 41% had two zones affected. This again suggests that all the practitioners were to an equal extent *x*-raying minor-symptom cases of a type that they would not normally send to the chest clinic. This conclusion is reinforced by the fact that the chest clinic first attendances in the area have not decreased as would be expected if the examinations made by the mass radiography units were only of patients who would otherwise have been *x*-rayed at the clinics. The "early" extent of the disease also confirms the impression that the patients examined in our scheme differ in type from those usually referred to chest clinics. Again, the rate for confirmed active tuberculosis (20 per 1,000) differs from the rate of tuberculosis in primary attenders at most chest clinics—that is, we are working in a different zone of diagnostic yield, the importance of which we have tried to measure in this paper.

Summary

A scheme offering unlimited chest *x*-ray facilities for general practitioners is described. Such a service could be provided in large towns if mass *x*-ray teams concentrated entirely on examination of general practitioners' cases.

The incidence of minor respiratory symptoms which are agreed by specialists to indicate the need for a chest *x*-ray film is so high in general practice that if the practitioner accepted the criteria and used the *x*-ray services available the clinics would be overburdened.

Early pulmonary tuberculosis mimics the symptoms of commoner minor ailments. It is a wolf in sheep's clothing.

These difficulties are well known to general practitioners, but the relatively narrow field of specialist experience has prevented the experts and the medical planners from being fully aware of them.

In general practice pulmonary tuberculosis is often diagnosed only on a "time" basis, after elimination of other causes, as distinct from "instantaneous diagnosis" by *x*-ray examination.

It may be objected that by offering unlimited *x*-ray facilities to general practitioners the profligate use of film is encouraged. No evidence of dilution was found to suggest that those doctors who used the scheme intensively had a lower discovery rate than those who *x*-rayed less often.

Figures are given for the incidence of pulmonary tuberculosis in patients referred with different symptoms or symptom-complexes.

Attention is drawn to the importance of radiological examination of unmarried people of both sexes who present with certain symptoms.

General practitioners must not feel disconcerted when many *x*-ray examinations yield nothing abnormal. This is the price of early diagnosis. The practitioner should use the miniature chest film with as little hesitation as he uses his stethoscope.

Tribute should be paid to the 183 general practitioners without whose enthusiastic participation the scheme could not have been started. We thank Dr. P. C. Anderson for advice and co-operation in the interpretation of films. We are also much indebted to the staff of the mass *x*-ray service for their indispensable assistance.

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The Department of Rheumatic Diseases of the West London Hospital has again with great promptness issued its annual report for the preceding year, and as usual it is full of interesting and useful information, including reports of original work. Of the patients who attended for treatment during the year, 33.2% were suffering from osteoarthritis, 12.8% from rheumatoid arthritis, 8.6% from the lumbar disk syndrome, 5.5% from capsulitis of shoulder, 3.2% from cervical disk syndrome, 2.6% from ankylosing spondylitis, 2.1% from psychogenic rheumatism, and 1.7% from gout. In his preface to the report Dr. W. S. C. Copeman, physician in charge of the department, mentions that gold salts are still found to be the most satisfactory single medicinal agent in the treatment of rheumatoid arthritis, and a large clinic, specially for these injections, has been organized. Research has continued into the most effective method of treating rheumatoid arthritis with cortisone and A.C.T.H.

TREATMENT OF BOWEL INFECTIONS OF THE TROPICS*

BY

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Bowel infections are notoriously prevalent in the Tropics, where they cause much morbidity in both the indigenous population and the European personnel serving there. The infections briefly can be divided into: (1) bacillary, (2) protozoal, and (3) helminthic. For most of these there is now available some reasonably effective treatment, and for some there is very effective specific treatment. It is with the specific treatment of a few of them that I propose to deal.

Bacillary Infections

Among the more important of the bacillary infections are the bacillary dysenteries and cholera; and typhoid, in view of the particular damage it causes to the bowel, may be added to them. The bacillary dysenteries and cholera are caused by infections which are localized within the bowel; in the former in the large intestine and in the latter in the small intestine. Typhoid is, of course, a generalized or systemic infection, and I do not propose to consider it as primarily a bowel infection.

The demonstrations by Marshall *et al.* (1941) of the efficacy of sulphaguanidine in the arrest and eradication of acute bacillary dysenteric infections in children in the United States was the beginning of the specific chemotherapy of the bacillary dysenteries. The findings of Marshall and his co-workers were rapidly confirmed by Fairley and Boyd (1943) on troops in the Mediterranean area, where bacillary dysentery had more than decimated the forces during the first world war. The speedy adoption by the British Forces of sulphaguanidine as a specific for the bacillary dysenteries was followed by the virtual disappearance of these diseases as a major cause of morbidity and mortality during the second world war. For a normal adult the dosage is an initial one of 6 g., and this is followed by 3 g. four-hourly, and then eight-hourly for two or three days into convalescence. The drug must not be continued for more than 10 days.

When sulphaguanidine was in short supply other sulphonamides, notably sulphapyridine, had been tried and been found also to be specific in the arrest of these infections. Their use in such a dehydrating febrile disease in a hot climate not uncommonly led to crystalluria and renal obstruction; where facilities were not immediately available to relieve this by ureteral lavage, deaths followed from uraemia. As a result the use of the freely absorbable and diffusable sulphonamides in the treatment of the bacillary dysenteries was discouraged among the British Forces, and the comparatively non-absorbable sulphaguanidine was adopted as the standard specific drug. Sulphaguanidine was followed in due course by other compounds with similar properties, of which succinylsulphathiazole and phthalylsulphathiazole are those most used. These are said to be even more effectively bacteriostatic than is sulphaguanidine, and in civil practice they now largely replace the sulphaguanidine of the war years. They are used in similar dosage.

The Americans have been less averse to the employment of the absorbable sulphonamides for the treatment of the bacillary dysenteries than are the British. There is some agreement that sulphadiazine is the most therapeutically

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effective sulphonamide for the treatment of the bacillary dysenteries. But those advocating its use emphasize the need for correcting dehydration and alkalinizing the urine before beginning treatment with it. There can be little doubt that at least under field conditions it is preferable to adhere to the British practice of using sulphaguanidine, succinylsulphathiazole, or phthalylsulphathiazole for treating cases of bacillary dysentery in all cases except under the stress of emergency. When sulphadiazine is used the dosage employed is up to 8 g. daily, in divided doses at four-hour intervals.

During the recent war years there was little evidence of the development of sulphonamide resistance by strains of the organisms causing bacillary dysentery. But Hardy (1946), in America, has recorded the development, by a strain of Flexner Z, of resistance to sulphadiazine. This development occurred in an institution for mentally defective children, in which successive cases of bacillary dysentery due to this organism were treated with subcurative doses of sulphadiazine, with the result that eventually this strain became completely refractory to the drug, and the course of the disease in the patients treated with it late in the epidemic was unchecked.

Hardy and Halbert (1948) treated a number of these children with streptomycin by the mouth. Given by this route streptomycin is not absorbed, and so it does not cause the toxic side-effects associated with its parenteral administration. They found that streptomycin was therapeutically beneficial in bacillary dysentery, but nevertheless it was much inferior to the sulphonamides; its only virtue in this connexion therefore seems to lie in its use in cases of infection with sulphonamide-resistant organisms, if these ever become prominent.

Cholera is an epidemic disease which ravages many parts of the East, and its effective treatment has so far been palliative along physiological lines. While claims have at various times been made that a number of drugs, in particular certain sulphonamides, act specifically in terminating the infection, none of these has withstood the test of time. Indeed, Lahiri (1951) indicates that, so far, the chemotherapeutic treatment of cases of cholera has proved detrimental to the patient rather than beneficial. In a fulminating infection of this kind, in which the vibrios multiply at incredible speed to a prodigious number throughout an extremely brief incubation period, it may well be that chemotherapy could only be employed too late to expect any benefit from it; and, apart from chemoprophylaxis, a specific drug treatment for the destruction of the organisms will not prove to be of value.

Protozoal Infections

The most important and geographically widespread of these is infection with *Entamoeba histolytica*; but, in addition, as localized infections of the intestine which may or may not cause clinical manifestations of their presence, there are lambliasis (giardiasis), trichomoniasis, and the much less common balantidiosis. Certain generalized protozoal infections such as kala-azar may secondarily implicate the bowel; but these hardly fall within our compass, and their treatment is that of the generalized infection.

Amoebiasis and amoebic dysentery (the terms are not synonymous) occur all over the world, and their precise relationship is uncertain. Hoare (1950) discussed the evidence for and against the view that all *E. histolytica* infections of man are pathologically active; he concluded that the parasite can and does live in the bowel commensally at times. If his opinion, which I share, is accepted, it can be argued that even in those persons who suffer from unmistakable relapsing attacks of amoebic dysentery the parasite may alternate between pathogenicity and commensalism. In view of its ubiquity it obviously is impracticable to detect, much less to attempt to sterilize, every case of infection with this parasite among the human populations of both the temperate and the tropical zones of the world. But nevertheless, rightly or wrongly, most clinicians feel it desirable, when circumstances allow, to sterilize of their infections persons found to be harbouring large cyst-producing races of the parasite, particularly if these persons have returned to temperate climates from a visit to the Tropics.

Infections with strains producing small cysts (below 10 μ in diameter) may be ignored in the absence of any convincing clinical manifestations to the contrary. To me it seems entirely unwarrantable, as is the practice of certain workers, more particularly in France and in the United States, to ascribe to an *E. histolytica* bowel infection an apparently limitless range of indeterminate symptoms remote from the abdomen; this especially when the patients have never been outside the moderate temperate zones, and have never even suffered from bowel troubles that could reasonably be attributed to the intestinal parasitization. One's credulity is stretched beyond the limit when anything from headache and visual disturbances to sexual disorders and rheumatoid arthritis have been ascribed to an otherwise symptomless *E. histolytica* infection solely on the grounds that specific treatment of the latter allegedly relieved these troubles.

Two Stages of Treatment

There are two stages in the treatment of an intestinal *E. histolytica* infection, and these are sharply distinct. First, there is the treatment of an acute attack of amoebic dysentery; secondly, as a sequel, there is the eradication of the bowel infection with the parasite. In addition to these, treatment in some cases may be necessary for an extra-intestinal infection with the parasite, such as an amoebic abscess of the liver.

For the treatment of an acute attack of amoebic dysentery emetine hydrochloride in doses of 1 gr. (65 mg.) given intramuscularly daily for a *few* days, is still unequalled. It has been stated that emetine is a dangerously toxic drug and that it always affects the heart. Its dangers have been grossly exaggerated. If a patient is kept in bed during the treatment and the drug is not given recklessly and in needlessly excessive dosage its dangers can with safety be completely ignored in ordinary practice. From three to six daily doses of the drug is all that is necessary to stop an acute attack of dysentery.

While emetine will unfailingly bring an acute attack of amoebic dysentery rapidly to an end, usually it will not sterilize the bowel of the infection, however unwisely the drug may be pushed or the course of treatment with it be prolonged. During the last few years some French workers have been pressing the claims of conessine, the active principle of kurchi bark, as a drug superior to emetine in the treatment of amoebic dysentery. Dispassionate observers studying the literature on the subject cannot fail to be unfavourably impressed by the unquestionable toxic side-effects of conessine treatment. Whereas emetine may affect the heart, conessine most certainly affects the head; indeed, it can cause very grave mental disorder, with maniacal symptoms, in persons unusually susceptible to the drug. The use of kurchi, or conessine, has almost been abandoned in India, where its employment over many years has largely been on the score of its ready availability there, and so its cheapness. There seem to me to be no adequate grounds for reviving it when emetine can be used; and, recently, informed French opinion appears increasingly to support this view.

When the acute attack of dysentery is controlled the next measure is to eradicate the basic intestinal infection before relapse of the dysentery can occur. For this, emetine by itself is ineffective, but a large number of compounds of extraordinarily divergent constitution have been advocated as effective specifics to achieve this end. Broadly, they may be classified as (*a*) compounds which contain emetine, of which E.B.I. (emetine and bismuth iodide) is the most generally used; (*b*) arsenicals, such as acetarsol, carbarsone, and the more recent milibis (a combination of arsenic and bismuth); (*c*) the iodo-oxyquinolines, such as "chiniofon,"

iodochlorhydroxyquin, and di-iodohydroxyquinoline; and very recently (*d*) the antibiotics, of which aureomycin and terramycin so far have proved the most effective.

Differences of Opinion

The claims put forward for any one of these drugs range in a remarkable manner from extreme optimism to extreme pessimism; and so the literature on them, in addition to being voluminous, is very confusing. After studying and attempting to analyse it, I find that the statements made by a large number of authors, writing of their experiences with them, are quite irreconcilable. One is driven to the conclusion that many of their statements are based on a lack of knowledge of the normal and possible courses of an *E. histolytica* infection and of the procedures necessary to determine its presence or absence. It seems to me that the most common cause of the confusion is a failure to examine efficiently for parasites an adequate number of specimens of stool after completion of a course of treatment with the drug under test. It should be common knowledge, as it is an unquestionable fact, that the number of parasites voided in the stools fluctuates from day to day and from week to week; often they are so scanty that none can be found for days on end.

From a considerable personal experience, I suggest that it is most unwise to infer that a person is free from *E. histolytica* infection of the bowel until at least ten or a dozen daily specimens of stool have been found to be free from parasites by a skilful technician regularly engaged in such examination. Even under such conditions, very occasionally a case of infection may escape notice; so, ideally, these serial examinations should be repeated at three-monthly intervals over a period of up to a year. While these standards obviously can but rarely be applied in ordinary medical practice, nevertheless adherence to them before statements are made about the efficacy of new and speculative amoebicides would do much to lessen the extravagance and inaccuracy of many claims and to obviate the resultant confusion in an already redundant literature.

Combined Use of Drugs

It has been the practice of British workers to combine the use of a number of the amoebicidal drugs over a period of two or three weeks when attempting to eradicate a bowel infection with *E. histolytica*. On the whole, in my opinion this practice has been thoroughly justified by the results. Some drugs, such as emetine, are absorbed from the bowel when given by mouth, and so presumably exert their action when conveyed systemically to parasites situated in the tissues of the bowel wall. Others, such as the iodo-oxyquinolines, are not absorbed to any appreciable extent; so presumably they exert their action locally within the lumen of the bowel on the parasites with which they actually come into contact. That emetine, when given by mouth, is absorbed from the gut, and therefore cannot be regarded as exerting its action locally, is evident by the cerebral nausea which rapidly follows its liberation within the bowel from good-quality enteric-coated tablets.

As an example of the second mode of action, may I cite the case of a man suffering from a very chronic form of true relapsing dysentery. He was given 16 tablets (nearly 3.5 g.) of di-iodohydroxyquinoline daily for three months, during which his stools were examined daily. No parasites at all were seen during this time, but after the drug was stopped they reappeared in the stools in large numbers within 48 hours. This suggests that the drug does destroy the amoebae with which it comes into contact within the lumen of the bowel, and so prevents their encystment and passage to the exterior in the stools. But under such circumstances the absence of parasites from the stools is not evidence of freedom from infection of the bowel; this is merely masked by the drug while it is being taken.

Within the last few years the antibiotics, particularly aureomycin and terramycin, have received much attention as therapeutic agents in infections with *E. histolytica*. The initial claim, which was based on an inadequate number of cases and insufficiently exacting standards of examination, was that aureomycin cured 100% of such intestinal infection. With further study by other workers this claim has been modified to a 50 to 80% cure rate. Terramycin has been stated to be at least as effective as is aureomycin and even less toxic; the general opinion is that it also will eradicate at least 70 to 80% of intestinal infections with *E. histolytica*. But Schneider (1951) has stated that though terramycin, like aureomycin, produces a satisfactory immediate clinical and parasitological response in intestinal amoebiasis, its effect its purely transitory, as clinical and parasitological relapse follow its use. Of 35 patients with amoebic dysentery, treated by Schneider with 2 g. of terramycin daily for 10 to 15 days, all relapsed parasitologically, and many clinically, within a few weeks of completing the treatment. Furthermore, he states that the drug was not always well tolerated, and in one of his cases it caused a marked rash.

Personal Observations on Aureomycin and Terramycin

In view of these remarkable discrepancies I venture to put forward some observations of my own on the uses of aureomycin and of terramycin in intestinal amoebiasis and amoebic dysentery. These are founded on the treatment of ex-members of the Forces with aureomycin or with terramycin, and their subsequent study and periodic re-examination over periods of at least three months and in some cases up to two years.

The treatment in each of these cases consisted in the administration of 0.5 g. of aureomycin by mouth six-hourly for 10 days, with no other accompanying drug treatment. Of 27 men treated with aureomycin, 23 were considered to be sterilized of their *E. histolytica* infections. Of the four cases which were not cured, in one case parasites were seen irregularly in the stools actually throughout the course of treatment; from the stools of the other three cases parasites were absent after the fourth or fifth day of treatment, but they reappeared within a week or two of its completion. Two of these four cases of failure to cure were those of men suffering from severe relapsing dysentery who had repeatedly been treated for some years with a remarkable and varied assortment of the usually accepted amoebicidal drugs: they were examples of the very refractory type of infection encountered from time to time. The subsequent re-treatment of all these four men with yet another combined course of amoebicidal drugs, and also a further course of aureomycin given concurrently with it, resulted in their successful sterilization as judged by regular re-examination over periods of from one to two years.

Forty-nine similar patients were treated with a comparable dosage of terramycin (0.5 g. six-hourly for 10 days); 46 of these 49 were considered to be cured by it. In one of the three cases of failure, parasites recurred in the stools irregularly during the treatment; in the case of the other two parasitological relapse followed within a week or two of treatment. Two of these three men were then cured by a combined three-weeks course of amoebicidal drugs given concurrently with terramycin. A third, after the initial unsuccessful terramycin treatment, was given a course of aureomycin alone; this failed to cure him. He then had a combined course of amoebicidal drugs without any antibiotic, which also failed. This combined course was repeated with the addition of aureomycin, and again it failed; but its repetition with terramycin instead of aureomycin resulted in the eradication of the infection, as judged by careful re-examination at three-monthly intervals for more than two years.

In no case was there any serious complaint of toxic side-effects from aureomycin or terramycin treatment in the dosages employed (20 g. over 10 days). Aureomycin not uncommonly caused a minor degree of gastro-intestinal upset, and occasionally a mild anal pruritus which in one or two instances persisted for some weeks. Terramycin

caused even less inconvenience to those treated with it. With neither drug was it necessary to curtail or to arrest the course of treatment as a result of toxic side-effects.

The results of treatment with aureomycin and terramycin therefore appear to me to be encouraging. It seems that treatment with either of the two will sterilize most of the average cases of amoebiasis encountered in practice. But these drugs are not infallible, and I do not think that in achieving the eradication of the infection they give results superior to those obtained with the combined course of treatment used so successfully in this country for many years. They are a most useful addition to the older amoebicides; and their especial value has been evident in those few cases of infection which have proved refractory to repeated courses of treatment with the older accepted amoebicidal drugs. The number of such cases, it is well to remember, is very small, but when encountered such refractory infections have hitherto constituted an apparently insoluble problem. These two antibiotics, when used as a supplement to the older amoebicidal drugs, seem to have provided the extra force necessary to eradicate these peculiarly resistant infections, and I value them accordingly. I would not recommend at present the indiscriminate employment of these antibiotic drugs in the ordinary straightforward case of amoebiasis, if only on the grounds of their considerable cost and their scarcity.

Summary

Two important bacillary infections in the Tropics are bacillary dysentery and cholera. Chemotherapy has not proved of benefit in cholera; it may be that it will not do so in the future in view of the extraordinary acuteness of the condition.

In the bacillary dysenteries sulphaguanidine and its successors, succinylsulphathiazole and phthalylsulphathiazole, are effective and are not prone to cause crystalluria and renal blockage. The absorbable sulphonamides, especially sulphadiazine, are also very effective, but renal obstruction may occur from their use.

Treatment of *Entamoeba histolytica* infection is discussed. The drugs accepted as being specifically amoebicidal include the alkaloids emetine and conessine, certain arsenicals, and the iodo-quinolines. Trials of aureomycin and terramycin show that these antibiotics are useful additions to the range of amoebicidal drugs. Their outstanding value appears to lie in their capacity, when given together with these drugs, to eradicate the extremely refractory infections occasionally met with.

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Burroughs Wellcome and Co. have made a new 16-mm. colour film (with sound) on the life cycle of *Schistosoma mansoni* and its laboratory maintenance entitled "The Human Blood Fluke." The film, which is in two parts each running for 16½ minutes, is intended for doctors, parasitologists, and pharmacologists. After a brief introductory sequence, the life cycle of the trematode is illustrated by living material and animated diagrams. Then follow details of the culture of the vector snail, *Australorbis glabratus*, and of the method of infecting mice with the cercariae. Lastly, the activities of various drugs against the disease in mice are compared. The film may be obtained from the Wellcome Film Library, 183–193, Euston Road, London, N.W.1.

THE CHEMOTHERAPY OF MALARIA AND TRYPANOSOMIASIS*

BY

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Malaria

The three synthetic antimalarials which had the most widespread use in the field until a year or two ago are mepacrine, pamaquin, and proguanil ("atebrin," "plasmoquine," and "paludrine"—as in every other field of chemotherapy, there is a confusing multiplicity of names for the same substance). These three drugs, although still extensively used, may now be regarded as the parent substances of classes of new and more effective drugs.

Mepacrine is of value as a suppressant but has no activity against the tissue stages of the malaria parasite. The closely related 4-aminoquinoline derivatives chloroquine and camoquin are now replacing mepacrine as malaria suppressants. Chloroquine was introduced by the Germans as "resochin," was developed in America as "aralen," and is also produced in France and Britain as "nivaquine." It is less toxic than mepacrine and does not stain the skin, and it acts a little more rapidly. It is now the drug of choice for the treatment of the malarial attack, although many workers still find a place for quinine in the treatment of the more severe cases (Covell, 1949). A dose of 300 mg. of chloroquine once weekly is enough in most areas for the suppression of malaria; this is the dose which is at present being used among sections of the United Nations Forces in Korea. The related compound camoquin is almost as good as chloroquine, and is being used chiefly in India, Egypt, South America, and the Philippines.

Pamaquin is not an outstanding schizonticide, and is of little value alone in the acute malarial attack. However, it has the property of killing the tissue forms of *Plasmodium vivax*. It has to be used with caution because of its toxic side-effects. Closely related 8-aminoquinoline derivatives have been prepared and tested in the United States; the best of them so far are pentaquine, isopentaquine, and primaquine. Primaquine is the primary amine corresponding to pamaquin, and is the best and least toxic of this series of drugs (Edgcomb *et al.*, 1950). It is now being used for the eradication of tissue forms of *P. vivax* in home-going United States Service men from Korea. When the men embark they are given a large dose (1 g.) of chloroquine to deal with any asexual parasites, and then a course of 15 mg. of primaquine daily for 14 days on the voyage home. This appears to be reducing very greatly the incidence of relapses of benign tertian malaria. The treatment therefore reduces the chances of re-establishing endemic foci of the disease in areas of the United States where anopheles mosquitoes capable of transmitting it still flourish (Public Health Reports, 1952). Even with primaquine, care is necessary because toxic side-effects occur in dark-skinned people.

Proguanil

Proguanil, which belongs to an entirely different class of chemical compound, has proved to be a very useful malaria suppressant, and in spite of the fact that inadequate treat-

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ment may give rise to resistant strains of malaria, there is little evidence of its having done so in most countries in which the drug has been used for the last six or seven years. A notable exception is Malaya, where Field and Edeson (1949) have found a gradually increasing resistance to proguanil treatment among the cases of overt malaria which are admitted to hospital. Resistance is caused by inadequate suppressant dosage, and is induced in the trophozoites but not in the tissue forms of the parasite (Cooper *et al.*, 1950). There is little chance of developing drug-resistance if sufficiently large and regular doses of proguanil are taken to suppress the blood parasites effectively, and, in any case, proguanil-fast strains are not resistant to mepacrine or chloroquine. Proguanil is a causal prophylactic against *P. falciparum*; it has some action upon the tissue forms of *P. vivax*, but is not a certain cure in every case.

It has been known for several years that proguanil itself has very little activity *in vitro* upon laboratory malaria parasites, but that serum from an animal treated with proguanil is active. This work suggests that the drug is changed in some way in the body of the host to produce an active metabolite. The nature of this metabolite was recently discovered by the workers at the laboratories of the Imperial Chemical Industries (Carrington *et al.*, 1951). It is formed by the cyclization of the biguanide chain of proguanil to form a diamino-dihydrotriazine derivative, which is about a hundred times as active as the parent substance in laboratory malaria infections. The introduction of a second chlorine atom into proguanil or into the triazine derivative produces even more active compounds which are at present undergoing clinical trial.

Pyrimethamine

Before the discovery of the metabolite of proguanil, Hitchings and his colleagues in the United States had been investigating the properties of diaminopyrimidine derivatives as antagonists of folic acid in cultures of bacteria. They found that proguanil was also a folic acid antagonist, and made the suggestion that diaminopyrimidines might therefore show antimalarial activity (Falco *et al.*, 1949). This was found to be the case, and a thorough investigation of a series of nearly 300 related compounds (Falco *et al.*, 1951) resulted in the introduction of a new antimalarial pyrimethamine ("daraprim"; "B.W. 50–63"). This drug has a chemical structure which resembles the metabolite of proguanil, and is somewhat more active against laboratory malaria infections. Clinical trials have been in progress in many parts of the world during the last 18 months, and the new drug appears to have considerable promise, especially as a malaria suppressant. A single dose of 5 mg. of pyrimethamine banished asexual parasites of *P. falciparum* and *P. malariae* from the blood of Lagos schoolchildren (Archibald, 1951). A weekly dose of 25 mg., given to all members of an isolated population in the Belgian Congo at the beginning of the rainy season, reduced the parasite rate in the people to zero after 15 doses, and the sporozoite rate in trapped anopheles mosquitoes to a very low level. Transmission of malaria was virtually at a standstill at the time of the year when it would have been expected to be proceeding at a very high rate (Vincke, 1952). Vincke is hopeful that courses of treatment with pyrimethamine may bring about a great reduction in malaria transmission over wide areas. In the treatment of the malarial attack, pyrimethamine has similar properties to proguanil, and has been found by most observers to be less rapidly effective than chloroquine.

Increasing attention is being given all over the world to the control of malaria by means of drugs, insecticides, and hygienic measures. In some areas notable progress has already been made in reducing the vast morbidity and mortality due to the disease, which was so vividly portrayed by Shortt (1951).

Trypanosomiasis

In the field of trypanosomiasis there have also been considerable advances in the last few years. The problem of treatment of human trypanosomiasis is threefold—the treatment of early cases, the treatment of advanced cases with involvement of the central nervous system, and prophylaxis. Early cases often respond satisfactorily to treatment with suramin ("Bayer 205," "antrypol") or pentamidine. Pentamidine is the least toxic and most effective trypanocide of the series of aromatic diamidines which were synthesized by Ewins and his colleagues at the laboratories of May and Baker. This work was a continuation of the studies upon long-chain diamidines carried out by King, Lourie, and Warrington Yorke. Pentamidine is very effective in the early stages of the disease, but it does not penetrate to the nervous tissue; it is therefore useless by itself for the treatment of advanced cases. Late cases are still treated with the arsenical drug tryparsamide, often together with pentamidine, and in many areas tryparsamide is still the mainstay of treatment.

Unfortunately, resistant strains of trypanosome are being encountered in some localities, especially in the Belgian Congo. It is therefore fortunate that a new series of potent arsenic derivatives has been introduced by Friedheim (1939, 1948, 1949). These are the melaminyl compounds, melarsen, melarsen oxide, and mel B. Perhaps the most promising of this series is mel B, which is a compound of melarsen oxide with dimercaprol ("B.A.L."), and which is less toxic than melarsen oxide itself. This substance is now manufactured by Rhône-Poulenc under the name of "arsobal." It is proving effective in the treatment of advanced cases even if they have failed to respond to tryparsamide, and a single dose is often enough to cure an early case of trypanosomiasis. The drug is not without its dangers, and some trouble has been encountered in the chemical preparation of batches which are uniform in toxicity. It is therefore essential that all batches of the drug which are manufactured should be controlled by biological tests similar to those laid down for the organic arsenicals used in the treatment of syphilis (Lourie, 1951). Toxic effects such as arsenical encephalopathy can be controlled by giving additional doses of dimercaprol until the arsenic has been excreted. Melaminyl arsenical derivatives produce resistant strains of trypanosome if insufficient drug is given, and these strains are also cross-resistant to all other arsenical drugs, including tryparsamide (Friedheim, 1951).

Another arsenical drug introduced in recent years is butarsen, which was selected for clinical trial after a great deal of careful laboratory work by Eagle (1945). Unfortunately butarsen is active only against early trypanosome infections, and is of no use when the central nervous system is involved. The drug is also of some value in the acute stage of South American trypanosomiasis caused by *Trypanosoma cruzi*.

For the prophylaxis of populations exposed to the risk of trypanosomiasis pentamidine is used. An injection will protect for a period of 4 to 12 months. However, it is very important that a full survey of the population should be made before the first dose is given, because some individuals are likely to be harbouring the disease already. Unless these are treated adequately with a full course of drugs, the infection may become cryptic and trypanosomes continue to live in nervous tissue without ever appearing in the blood or lymph-node juice. The opportunity for curing such patients easily will then have been missed.

Cattle Trypanosomiasis

Shortt (1951) has stated that he considers "the trypanosomes affecting man's domestic animals to be far and away more important [than human trypanosomiasis] when the whole picture is looked at in perspective." This is because animal trypanosomiasis denies at least a quarter of the land surface of Africa to all domestic animals except poultry. A number of drugs have been introduced during the last 10 years which give reason to hope that in the future it may be possible to utilize at least the marginal areas of the tsetse belts for the grazing of cattle, and it is already possible to transfer cattle through fly country from one safe area to another, under cover of a protective injection of a drug.

Before 1938 the only substance of any value in the treatment of *Trypanosoma congolense* and *T. vivax* infections in

cattle was tartar emetic. The Germans introduced "surfen C," which was effective but toxic, and shortly afterwards Walls synthesized the first of the phenanthridinium compounds (Browning *et al.*, 1938), which have since been widely used for the treatment of *T. congolense* and *T. vivax* infections. The most effective substance of this series was, until recently, dimidium. Unfortunately this drug has a severe locally irritant action, and sometimes produces damage to the liver, which may lead to a condition resembling photosensitization of the skin, appearing five to six weeks after the dose. In 1949 "antrycide" was introduced, and it looked for a time as though at last an effective remedy had been found, both for the treatment of infected cattle and for the prophylaxis of animals grazing in fly areas (Davey, 1950). "Antrycide" is a very good drug, but, like all other chemotherapeutic substances, it has its limitations. It produces toxic side-effects in ill-fed animals, and in areas of heavy fly density an injection of antrycide prophylactic will protect only for a period of two months (Unsworth, 1951). In the wilder parts of Africa it is not possible to give protective inoculations at short intervals, and antrycide prophylactic does not exert its action for long enough to make it very suitable for use in this way. However, for the purpose of grazing animals for limited periods in marginal territory, and for the passage of cattle through the fly belts on their way to market, the drug has very real uses (Unsworth and Birkett, 1952). Antrycide-resistance is easy to produce, and resistant strains of trypanosome are cross-resistant to the phenanthridinium compounds.

A new phenanthridinium compound has recently been prepared and tested by workers in the laboratories of Boots at Nottingham. This is "ethidium," which has an ethyl group instead of a methyl group associated with the quaternary nitrogen atom (Watkins and Woolfe, 1952). Ethidium is claimed to be less toxic and more active than dimidium, and preliminary trials in the field have been encouraging. A number of other phenanthridinium derivatives are still undergoing trial, and a trypanocidal cinnoline compound is soon to be tested in the field (Lourie *et al.*, 1951). The frequency with which new organic compounds are being presented for trial in the field gives promise that it may not be long before cattle trypanosomiasis is brought under control. Investigations are also being made upon the breeding of races of cattle which show increased natural tolerance to the disease, and it may be that this method, and not the injection of chemical poisons, will prove to be the real answer to the establishment of cattle in the tsetse areas.

Summary

Developments in the chemotherapy of malaria are discussed, together with the qualities of the various antimalarial drugs.

The treatment of human trypanosomiasis and the question of mass prophylaxis are surveyed.

The importance of the treatment of cattle trypanosomiasis is emphasized, and the value of new drugs used for this purpose is assessed.

Mention is made of the employment of antrycide as a short-term prophylactic in cattle.

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SUCCESSFUL LACTATION IN ADDISON'S DISEASE

BY

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Successful pregnancy in a woman suffering from Addison's disease has often been reported, but successful lactation would seem to be a rare event. It is therefore thought worth while to report a case in which delivery of a healthy infant was followed by the establishment of successful breast-feeding.

Literature

A search of the literature since replacement therapy has been used has shown several reports of successful pregnancy; in some of these no mention is made of lactation, in others slight congestion of the breasts was noted a few days after delivery, and in yet others attempts at breast-feeding were not permitted. Fitzpatrick (1922) reported the successful delivery of a patient in whom Addison's disease had been diagnosed during the pregnancy; he did not, however, mention lactation. At the same time he reported 11 cases from the literature in which Addison's disease had complicated either pregnancy or the puerperium, but in none of which both mother and infant had survived. A further case of successful delivery was reported by Perkins (1932), but breast-feeding was said not to have been permitted. Maranon (1936), in a review of sexual function in 169 cases of Addison's disease, 88 of them women, stated that pregnancy was less likely to occur in those suffering from Addison's disease, but that when it did occur death of the woman during pregnancy or soon after delivery was not uncommon. He agreed with the opinion expressed by Rowntree and Snell (1931) that in most women suffering from Addison's disease mammary atrophy occurred, and that this was the reason why breast-feeding of the infant was not possible.

Galloway *et al.* (1940) reported the successful delivery of a full-term infant in a case in which the pregnancy had been complicated by an acute suprarenal insufficiency. Van Zwanenberg (1945) reported two cases in which symptoms of Addison's disease occurred during pregnancy; one of these patients died during the fourth month following hysterotomy and sterilization, while the second responded to "eucortone" therapy and a live child was obtained. In this case the infant was not put to the breast and no attempt was made to inhibit lactation, but, except for some hardening of the breasts on the third and fourth days of the puerperium, there were no signs of lactation. The case of a woman suffering from Addison's disease who had two successful pregnancies was reported by Leonard Simpson (1946). He suggested that lactation might have occurred if treatment had been different, cortical extract containing the carbohydrate factor being used instead of deoxycortone.

Knowlton *et al.* (1949) described five pregnancies, in only two of which was a live infant obtained. In the first case delivery was by caesarean section and the child lived only 24 hours. In both these cases engorgement of the breasts was observed a few days after delivery, but it is noted that in the case in which the child survived no attempt was made at breast-feeding, and by the seventeenth day after delivery the breasts were soft and had only a slight watery discharge. Brent (1950), in a general review of Addison's disease and pregnancy, collected 39 cases from the literature and described a case of her own in which delivery was by caesarean section, the woman dying four days later. She stated that lactation rarely occurred, but that if it did it should be suppressed, and mentioned the opinion held by one author who thought that lactation might precipitate an adrenal crisis. She concluded by saying that caesarean section was not to be recommended in cases of Addison's disease.

The following case report describes successful delivery by caesarean section one week before term, the establishment without difficulty of lactation, and the continuance of breast-feeding until the child was 4 months old.

Case Report

A woman aged 20, Italian by birth, was admitted to hospital on August 17, 1948, complaining of increasing lassitude and pigmentation of the body. At this time she was thirty-two weeks pregnant, and the symptoms had been gradually increasing since the fourth month of pregnancy. On inquiring into the past history it was found that Addison's disease had been diagnosed two years previously in Italy, and that treatment with cortical extract over a period of some months had led to a marked amelioration of the symptoms. Further inquiry revealed the fact that the patient's grandmother, and both an aunt and an uncle on her mother's side, had died of pulmonary tuberculosis. The patient herself had a pyrexial illness, accompanied by loss of weight, six years previously, which was diagnosed as "pleurisy." The menstrual periods had been normal; the only other pregnancy, in 1945, had ended in a miscarriage at six weeks.

On examination her general condition was good, but there was a pronounced brown pigmentation of the face, involving particularly the forehead, nose, and malar regions, and of the trunks, limbs, and buccal mucosa. The blood pressure was 100/50. The other systems were normal. The blood sodium was 265 mg. per 100 ml.; blood chlorides 604 mg. per 100 ml.; and blood potassium 23.8 mg. per 100 ml. An *x*-ray film of the chest showed no abnormality. A straight *x*-ray film of the abdomen showed breach presentation with extended legs; no calcification of suprarenals, and no calcified mesenteric glands. An *x*-ray film of the skull showed that the pituitary fossa was of normal size.

Treatment was begun on August 24 with sodium chloride, 2 g. thrice daily; five days later the blood pressure had risen to 110/68. At the end of a week deoxycortone, 5 mg. daily, was given in addition to the sodium chloride, and was increased gradually to 5 mg. thrice daily. At the end of four weeks the patient was feeling very much better, the pigmentation was less pronounced, and the blood pressure was 116/84. At this time, as the presentation was an extended breech and attempts at version had failed, it was decided to deliver the patient by caesarean section, and at the same time to sterilize her. One week before term, therefore, classical caesarean section was performed under local analgesia and gas and oxygen. A living male child, weight 6 lb. 8½ oz. (3.1 kg.) was delivered. The post-operative progress was uneventful. The blood pressure fell to 90/70 immediately after delivery, but rose gradually to 142/92 on the seventh day. Drug therapy was continued as before delivery. Lactation was established without difficulty; the infant was put to the breast on the day of delivery and sucked well. With the exception of a small complementary feed on the third and fourth days, the infant was wholly breast-fed until 4 months of age. On the twelfth day of the puerperium deoxycortone acetate, 300 mg., was implanted into the abdominal wall. The patient was discharged from hospital on the seventeenth day symptom-free, and with a blood pressure of 142/92. When she was seen in the out-patient department four weeks after discharge she was feeling well and doing all her own housework in addition to feeding the infant; pigmentation was less, and the blood pressure was 162/90.

She continued well and symptom-free until the child was 4 months old, when she again complained of lassitude. Since the baby was then a lusty child who would suffer no ill effects from artificial feeding, breast-feeding was discontinued, with rapid relief of symptoms.

The patient remained under observation, having been given a maintenance dose of 5 g. of sodium chloride daily, until the child was 1 year old. At this time she complained again of lassitude and also of increased pigmentation. On inquiry it was discovered that she had recently omitted to take her sodium chloride. A second implant of 300 mg. of D.C.A. was given in September, 1949, and a third implant in October, 1950. She was last seen in November, 1950, when she was again symptom-free and doing all her own housework as well as looking after her 2-year-old child; the blood pressure was 130/80.

I wish to thank Dr. A. Margaret Macpherson and Miss Gladys Hill for their interest and help in the preparation of this paper and for permission to publish.

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NEONATAL MYASTHENIA GRAVIS

REPORT OF A CASE

BY

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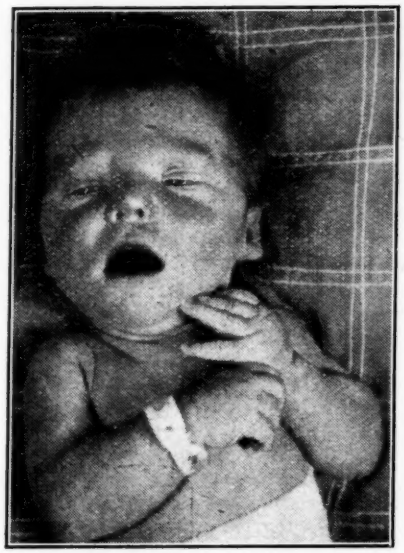
Twelve cases of myasthenia gravis occurring in newborn infants of myasthenic mothers have been reported (Strickroot *et al.*, 1942; Wilson and Stoner, 1944; La Branche and Jefferson, 1949; Levin, 1949; Nilsby, 1949; Stone and Rider, 1949; Geddes and Kidd, 1951; Holt and Hansen, 1951; McKeever, 1951). In view of the rarity of the condition we think it justifiable to present a further case.

Case History

The mother, a primigravida aged 40, had been diagnosed as suffering from myasthenia gravis at the age of 38, though she had experienced intermittent symptoms since the age of 12. Her myasthenia was well controlled on oral neostigmine, 15 mg. q.d.s., atropine 1/100 gr. (0.65 mg.) b.d., and ephedrine, 1/6 gr. (11 mg.) q.d.s. There were no exacerbations of her symptoms during pregnancy nor did remissions warrant the discontinuation of her treatment. She was delivered by caesarean section (Mr. A. L. Gunn) because of uterine inertia. Her post-operative and puerperal course was uneventful.

The infant, a boy, weighed 6 lb. 2 oz. (2.8 kg.). His general condition and colour were good at birth, but a few hours later he was found to be drowsy, had a feeble cry, and would not suck. On the second day his sleepiness was more pronounced. His face was expressionless even after painful stimuli, and he could not open his eyes fully. There was no tone in his neck muscles, so that his head lolled about, his jaw sagged, and he was unable to close his mouth (see illustration). Mucus collected in his throat and had to be aspirated. Sucking was impossible as his mouth hung open, and spoon feeds were regurgitated. The myasthenia was most evident in the muscles of the face. Spontaneous limb movements were infrequent, but the Moro reflex was present. Respirations were normal, and he was never cyanosed. There was no radiological evidence of thymic enlargement on the fourth day of life.



Because of the infant's inability to suck, feeds were given by oesophageal tube. On the fifth day 0.05 mg. of neostigmine was injected intramuscularly without improvement. He was then started on oral neostigmine, 3 mg. half an hour before each feed, and atropine, 1/200 gr. (0.32 mg.) four-hourly. A slight improvement occurred when the dose of neostigmine was increased to 3.75 mg. orally before each feed.

It was our impression that the improvement in muscle tone was not clearly related to the medication, which was therefore discontinued on the eleventh day. The myasthenic symptoms steadily cleared, but the child did not regain his birth weight until the twenty-third day. On that day he presented no abnormal signs, the thymus was not visible in a chest radiograph, he took well from the bottle, and he was discharged to the follow-up clinic. On the sixty-seventh day he weighed 9 lb. 12 oz. (4.5 kg.), his central nervous system and musculature were normal, and the curare test of Bennett and Cash (1943) was negative.

Aetiology of Myasthenia Gravis

In myasthenia gravis the transmission of nerve impulses to the muscle plate is impaired. The nature of this defect of transmission is unknown. According to Wilson and Stoner (1944) and Keynes (1949) a curare-like substance is formed as a by-product of acetylcholine breakdown, or is liberated by the thymus. This substance seems to reduce the available acetylcholine or to raise the threshold of the myoneural junction to acetylcholine. There is no evidence for the alternative theories that the liberation of acetylcholine at the neuromuscular junction is deficient, or that the action of acetylcholine is impaired by abnormal cholinesterase activity (Wilson *et al.*, 1951).

All children reported as showing myasthenic symptoms at or shortly after birth were the offspring of mothers suffering from myasthenia gravis. Two of these infants died soon after birth; the others recovered spontaneously or with treatment. All but one child needed no further treatment after the first few weeks of life, and there is no evidence that in his case cessation of treatment would have led to recurrence of symptoms.

At first sight it seems reasonable to suppose that the symptoms in the child are due to the transplacental passage of a curare-like substance from the myasthenic mother to the infant. These symptoms continue until this substance is destroyed in some manner during the first weeks of life, leaving the child unaffected later on. This theory, however, would seem to be untenable, as the great majority of myasthenic mothers give birth to normal children. Levin (1949) postulates a latent genetic sensitivity in the child which, in conjunction with the curare-like substance, leads to "neonatal" myasthenia in the offspring of some myasthenic mothers. Susceptible children with normal mothers would remain asymptomatic unless another factor, such as an infection, precipitates an enduring "congenital" myasthenia in infancy. Five such cases have been reported (Rothbart, 1937; Bowman, 1948; Levin, 1949; Mackay, 1951). All these children had normal mothers, their symptoms were not transient, and the diagnosis of myasthenia starting soon after birth was presumptive and retrospective, as they were not seen by the authors until later in life.

Levin (1949) suggests that "neonatal" and "congenital" myasthenia may differ only in degree. It seems to us, however, that the transient neonatal cases must be fundamentally different from those arising some time after birth and remaining permanently. The latter cases are clearly straightforward instances of myasthenia gravis occurring early in childhood, similar to those reported by Levethan *et al.* (1941), Kawaichi and Ito (1942), Ford (1944), Keynes (1949), and Wyllie *et al.* (1951).

The different clinical course of the two types of myasthenia strongly suggests that they are different in causation: in the transient kind the symptoms, distribution of paralysis, and course are strikingly similar, in marked contrast to the variable symptoms, the asymmetrical paralysis, and the unpredictable course of the disease in the patient with permanent myasthenia.

Secondly, Levin's theory does not account for the fact that not one of the neonatal cases developed permanent myasthenia gravis later in life, when their supposed inherent susceptibility would be expected to be activated, in some cases at least, by intercurrent infections, etc.

Lastly, not one of these children who had a transient myasthenia has been reported as having a positive curare test after recovery. If an inherent susceptibility existed it would surely have been revealed by this test.

Summary and Conclusions

A case of transient myasthenia in the newborn child of a myasthenic mother is reported. Twelve previously recorded cases are summarized and the literature is reviewed.

Normally, curare does not cross the placental barrier (Buller and Young, 1949; Harroun and Fisher, 1949). This presumably also holds for the curare-like substance responsible for the symptoms of myasthenia gravis. Therefore most myasthenic mothers give birth to normal infants. However, the placenta sometimes allows substances to pass which are usually retained. This altered permeability is due to changes in the chorion epithelium (Schlossmann, 1932), and results in the occasional approximation of the maternal and foetal blood streams (Huggett, 1946–7).

We suggest that infants showing transient neonatal myasthenia are essentially normal, that they receive a curare-like substance from their myasthenic mothers via a defective placenta, and that their myasthenia disappears, never to return, when this substance has been destroyed.

We wish to thank Dr. J. M. Piney, consultant anaesthetist, Lewisham Hospital, for carrying out the curare test, and Miss Ellis, of the Lewisham Group Laboratory, for the photograph.

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Medical Memoranda

Massive Fat Embolism Following Fracture of the Femur: Complete Recovery

Fat embolism occurring as a complication of fracture of the femur is said to be comparatively rare. Wilson and Salisbury (1944) found eight cases of clinical fat embolism in 1,000 consecutive battle casualties, with a mortality of 75%. Cases of fat embolism have been classified into pulmonary, systemic, and combined types. The combined type (systemic and pulmonary) is said to be invariably fatal. We would like to place on record a case of the combined type which clinically justified the diagnosis of fat embolism, with complete recovery.

The subject of fat embolism has been extensively reviewed by Scuderi (1934, 1938, 1941), Watson (1937), Harris *et al.* (1939), Rowlands and Wakeley (1941), Robb-Smith (1941), and Robb-Smith *et al.* (1942). In all over 600 cases have been described.

CASE REPORT

A man aged 32 was admitted to hospital on October 25, 1948, after having been struck by a lorry which mounted the pavement after a collision.

On admission he was suffering from shock. There was deformity of the left thigh due to a fracture of the femur which was confirmed by *x*-ray examination. A Steinmann pin was inserted through the tibial tubercle under gas, oxygen, and ether anaesthesia by one of us (B. S. S. A.), a Thomas splint put on, and extension applied. Next day the temperature rose to 102° F. (38.9° C.) and the pulse rate to 110.

The patient was confused and restless. As careful examination did not reveal any other cause for the sudden change in his condition, a provisional diagnosis of fat embolism was made. This was supported by the finding of a number of fat globules in the urine. During the day he lapsed slowly into coma and his general condition deteriorated.

On October 27 he was still unconscious, and was fed by a nasal tube. He had a diffuse petechial rash all over his chest and abdomen, and his pupils were dilated and fixed. White rounded patches were visible on the temporal side of the right optic fundi. Rales were present at the bases of both lungs, being most pronounced on the right side. Both upper limbs and the right lower limb were spastic, and on the right side the reflexes were exaggerated; there were also ankle clonus of the right side and a bilateral extensor plantar response. The *x*-ray report on the chest on October 27 was as follows: "There are signs of bronchopneumonia of both the lungs, affecting chiefly the right base."

On October 29 the patient began to take fluids by mouth. The spasticity of the limbs was now much lessened, and the lungs were clear except for a few scattered rales over the base of the right lung. *X*-ray examination of the chest on November 1 showed the lung fields to be almost clear. By November 10 (the sixteenth day) the patient had made a complete recovery.

COMMENT

The diagnosis of fat embolism should not present any difficulty. The signs one should look for are any of the following: petechiae over the trunk, spasticity or paralysis of one or more limbs, exaggerated tendon reflexes, extensor plantar response, signs of bronchopneumonia within 24 hours of an accident, and fat globules in the urine. This case is of particular interest because the fat embolism was massive, yet the patient not only survived his illness but was also left with no residual paralysis or weakness.

We wish to express our thanks to Dr. O. W. Roberts, medical superintendent of Dulwich Hospital, for permission to publish this case.

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Vaginal Jellies: How Long they Stay in the Vagina

Tests have been made on 17 women attending a V.D. clinic to ascertain how long an application of vaginal jelly will stay in the vagina. For this purpose a 6% "modocol" jelly, the ethyl-cellulose base used in most of the Kylon preparations, with 2% starch as an indicator, was kindly prepared by the manufacturers.

A preliminary *in vitro* test was undertaken with a tincture of iodine diluted with water to 0.5% on the commoner vaginal applications in use in the clinic. When the iodine was added to chloramphenicol pessaries, carbarsone pessaries, or acetarsol powder no reaction was noted. An intense blue colour was, however, observed when it was added to acetarsol tablets, and care was taken not to employ them for the women under observation in this series.

The patients chosen were 15 white and 2 negro women of an average age of 27 years (extremes 14–38). The conditions from which they were suffering were: vaginitis, 4; salpingitis, 2; oedema of the vulva and vulvitis, 2; cervicitis, 2; gonorrhoea, 2; fluor albus, 2; thrush, 1; sterility, 1; anxiety, 1.

The vagina of each was first swabbed with cotton-wool, and 0.5% iodine was then poured over the moist swab. No blue colour was noted. The modocol jelly containing starch was then inserted with a Kylon extendable applicator, a form of cardboard syringe which will hold 5 g. of jelly. The iodine test was repeated after 1 to 14 days. The results were as follows:

Days:	1	2	3	4	5	6	7	13	14
Positive..	1	1	3	1	—	—	—	—	—
Doubtful	—	—	—	2	—	—	—	—	—
Negative	—	—	—	2	1	1	3	1	1

Thus of five patients tested at one to three days all showed starch present in the vagina. The results of those tested on the fourth day were indefinite, while of seven tested at five or more days starch was present in none.

The cardboard applicator proved an efficient instrument for introducing the jelly into the vagina.

I am grateful to Kylon Ltd. for kindly providing the jelly and applicators used in these tests.

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Reviews

LUMBAR DISK LESIONS

Lumbar Disc Lesions: Pathogenesis and Treatment of Low Back Pain and Sciatica. By J. R. Armstrong, M.D., M.Ch., F.R.C.S. Foreword by H. Osmond-Clarke, C.B.E., F.R.C.S. (Pp. 240; illustrated. £2 2s.) Edinburgh and London: E. and S. Livingstone. 1952.

The need for an eclectic sifting of the vast literature that has accumulated in recent years on the subject of lumbar intervertebral disk lesions has been apparent for some time, and Mr. Armstrong has achieved this successfully in his monograph. He also contributes a number of his own opinions and observations.

He covers the whole subject of lumbar disk lesions in an exhaustive manner. The earlier chapters include sections on the anatomy, physiology, and function of the disk, and in the later chapters he gives a good description of the pathology and clinical features of prolapse. Some statements on neurological points are open to dispute—for instance, those on the value of the ankle-jerk in the localization of the affected nerve root and on the considerable dangers associated with lumbar puncture. But these are minor criticisms of an otherwise well-balanced presentation. He discusses in great detail the differential diagnosis, and numerous pathological conditions of the spine and ligaments receive individual attention. Some controversial features, such as the use of myelography in diagnosis and the performance of spinal fusion at the time of disk exploration, are particularly well summed up. The results of operative treatment are perhaps rather superficially surveyed, and the value of this chapter would have been enhanced if the author had included the results of his extensive experience of more than 1,000 operations for disk lesions.

For the surgeon well versed in the treatment of disk protrusion the book does not contain many strikingly new facts or observations; it should be regarded as an advanced textbook, and as such sets out views on pathology and treatment representative of the opinions of most orthopaedic and neurological surgeons in Britain. It should soon become the standard work on the subject. The book is well produced and generously illustrated with *x*-ray reproductions of good quality and a large number of excellent diagrams and drawings, many of them in colour.

V. LOGUE.

RELAXATION IN PSYCHOTHERAPY

Muscle Relaxation as an Aid to Psychotherapy. Volume 1. By Gerald Garmany, M.B., Ch.B., M.R.C.P., D.P.M. Physical Medicine Series Volume 1: General Editor, William Beaumont, M.R.C.S., L.R.C.P. (Pp. 65; 5s. 6d., paper edition 3s. 6d.) London: The Actinic Press. 1952.

Nervous tension is largely responsible for the fact that phenobarbitone is now replacing bromide as one of the widely prescribed drugs in medicine. Our national budget, too, depends for its stability on alcohol and tobacco supplying other remedies for tension. Months of psychotherapy may prove fruitless in bringing relief, and nearly ten thousand leucotomies have been done in this country on patients in most of whom this symptom has been prominent and led finally to total breakdown. Any method helping to combat it, therefore, needs careful investigation.

Jacobson, in the U.S.A., has spent many years in working out and popularizing a system of controlled muscle relaxation which is often accompanied by relief of tension. This book outlines a similar method which may be taught by the physiotherapist, preferably accompanied by guidance given to the patient by a psychiatrist experienced in the method. Though the reviewer has no experience of such methods, he can vouch for intelligent persons who find they have been greatly helped.

The author of this book is careful not to claim the method as a panacea. He does not advise it in those with dissociative hysterical personalities, who we know can often be helped by psychotherapy, hypnosis, and abreaction. But he does stress its efficacy for patients with tense, obsessive, and driving personalities, who are notoriously difficult to help with other forms of psychiatric treatment. If these findings are confirmed in this group alone, a therapeutic weapon of considerable value will be placed in the hands of doctors. And physiotherapy departments will, unfortunately, become more overcrowded than ever.

This small book contains detailed instructions for the physiotherapist on the part she has to play, and endeavours to put the method in its proper medical setting. As Dr. William Beaumont remarks in a foreword, "The reader will find a clear explanation of what to do, how to do it, and why it is done."

WILLIAM SARGANT.

THE YOUNG DELINQUENT

Juvenile Delinquency. By J. D. W. Pearce, M.A., M.D., F.R.C.P.Ed. (Pp. 396. 25s.) London: Cassell and Co. 1952.

Saving Children from Delinquency. By D. H. Stott, Ph.D. (Pp. 266. 12s 6d.) London: University of London Press. 1952.

Dr. Pearce describes his volume as "a short textbook on the medical aspects of juvenile delinquency." Delinquent actions are regarded as symptoms, but by no means the only symptoms, of four main types of mental disturbance. These in turn are presumed to arise from four main sources of mental tension—the acquisitive tendency, the aggressive tendency, the sexual tendency, and the tendency to escape from unpleasant situations. In any individual case, however, the aetiology is likely to be highly complex, and usually involves not only factors in the child but also factors in the child's environment. A consideration of these predisposing causes leads Dr. Pearce to put forward a working classification consisting of nine subgroups or categories, "each fundamentally different from the others." A separate chapter is devoted to each category; and the volume concludes with a detailed account of the more effective methods of treatment and prevention, with special reference to the help that the general practitioner can give.

Doubtless owing to considerations of space, Dr. Pearce does not offer detailed evidence for his special views on classification or causation, or on the efficacy of the different types of treatment that he advocates. There are, too, a number of slips which might perhaps be corrected in a second edition. "Intelligence quotients" and similar devices were used in clinics for diagnostic purposes long before "World War II." Dr. H. H. Goddard, who is described as an "outstanding contributor" to the psychology of delinquency "in this country," was head of the Vineland Institution for the feebleminded in the United States. Nevertheless, in spite of minor defects, the book will be both helpful and welcome to the growing number of medical practitioners whose assistance is sought by parents, magistrates, or teachers, and who have neither the time nor the inclination to study more technical expositions.

Dr. Stott's book is a supplement to his fuller report on *Delinquency and Human Nature.* He describes it as "an essay rather than a psychological treatise." It consists largely of articles previously published in *The Times Educational Supplement* and *Probation,* but revised for the present work. Two of the most interesting chapters are those which describe the existing organization of approved schools and the radical changes which Dr. Stott thinks should be introduced: both are based on first-hand experience. In the main, however, his discussions are addressed to parents and the general public rather than to the medical, psychological, or administrative expert, and his aim throughout has been to awaken a more active interest rather than to report detailed results or scientific conclusions.

CYRIL BURT.

BRITAIN'S FOOD

Britain's Food Supplies. By K. G. Fenelon, M.A., Ph.D. (Pp. 212. 15s.) London: Methuen. 1952.

During recent years we have been made all too familiar with the lesson that only half of Britain's food supplies can be produced at home. The rest must be imported, and paid for in manufactured goods, coal, or services. It has been emphasized that changes in the relative values of manufactured and agricultural products have increased our difficulty in balancing our accounts. Our progress, and even our survival, may depend upon our willingness to accept present sacrifices in order to secure future benefits.

Mr. Fenelon, who was once director of statistics and intelligence at the Ministry of Food, should therefore be congratulated and thanked for compiling a concise, well-informed, and carefully documented book which clearly indicates the necessity for such sacrifices. After looking back on our food supplies in the eighteenth century in a historical introduction, he proceeds to examine the effect of the two world wars, and to discuss the official steps taken to prevent hunger and malnutrition. He gives details of the variations of our sources of food in the second world war, which were profoundly altered by the substantial supplies which we received from America. Chapters deal with rationing schemes, the purchase of food by the Government, communal feeding, the world's food supplies, international organizations, and schemes for development in the Commonwealth and Colonies. A statistical appendix and numerous tables and charts repay careful study. It seems remarkable that the average member of our population spends more on tobacco and alcohol than on housing, and that the whole of Africa produces only about one-tenth as much grain as is produced in Europe.

After food has been idealized so often as a symbol of social progress it is refreshing to meet an author who is content to treat his subject objectively, without displaying any political or moral bias. His reward should be the earnest attention of all who are concerned, either directly or indirectly, in shaping the country's future.

T. MOORE.

ELECTROCARDIOGRAPHY

Manual of Electrocardiography. By Benjamin F. Smith, M.D. (Pp. 215; 119 figures. £1 12s.) London: Cleaver-Hume Press. 1952.

Clinical Electrocardiography. By Dr. Max Holzman. Translated by Douglas Robertson, M.A., D.M., M.R.C.P. Second edition. (Pp. 647; illustrated. £5 5s.) London: Staples Press. 1952.

A Manual of Electrocardiography, by B. F. Smith, is intended to be a simple and practical introduction to the subject. The author does not attempt to cover the whole field. In the chapter on the electrocardiograph he goes into the physics of one type of machine too fully, for nowadays string galvanometers are not so generally used. The chapter on the theory of the production of the electric field of the heart is good; the description of a volume conductor and the electric dipole is clear, and there are some informative diagrams. Depolarization and repolarization are well described and the current of injury is here mentioned, rather too soon one would say. After this there is not much to praise. The photographs of the position of the heart all look very much alike; in any case the electrical position correlates but poorly with the anatomical, so they are really superfluous. The illustrations of the cardiograms are throughout unsatisfactory. It is unnecessary to give seven complexes of standard lead I. The unipolar leads are represented joined on, so one cannot easily see where one ends and another starts. The letterpress is often obscure, and a chapter called "Pen Pictures of Cardiology" is neither to the point nor useful. The clinical descriptions are inadequate. There is an unsatisfactory chapter on the correlation of electrocardiograms with findings at necropsy. The descriptions of the necropsies are poor and full of irrelevant material. In all, this book is not up to the level of many other simple introductory handbooks; the approach is old-fashioned in many respects and often far from simple.

The second edition of *Clinical Electrocardiography*, by Max Holzman, of Zurich, has been translated by Douglas Robertson. For the most part this reads well, but at times there are obscurities, some present in the original German, and at times the expression tends to be clumsy and lacks fluency. There is the conventional beginning with the old standard limb leads, but a novelty lies in the discussion of the cardiac vectors in relation to them. This appears to be sound in idea and is clearly done, but no doubt would make heavy going for a novice. The chapter on bundle branch block is rather complex, and "arborization block" receives much consideration. Auricular fibrillation and flutter are still discussed under the theory of "circus movement"; except for a footnote by the author, the work of Prinzmetal is not mentioned.

This volume is very comprehensive; every aspect of the clinical application of electrocardiography finds a place, and the information is presented in a practical and logical manner. After each section there is a full list of up-to-date references. The illustrations are all excellent, and the type and paper of the first quality. One can fully recommend this volume to anyone who needs a very full and modern survey of this subject, which is now assuming very large proportions. One begins to wonder whether the cardiographic tail is wagging the cardiological dog.

TERENCE EAST.

THE BIRMINGHAM HOSPITALS CENTRE

The Birmingham Hospitals Centre. By Stanley Barnes, M.D., D.Sc., F.R.C.P., (Hon.)LL.D.Birm. With foreword by Sydney Vernon, LL.M. (Pp. 144; illustrated. 15s.) Birmingham: Stanford and Mann, Ltd. 1952.

The magnificent buildings which form the Birmingham Hospitals Centre arouse the admiration of all who see them, but few outside Birmingham are aware of the hard struggle which went on for several years before conflicting interests could be reconciled sufficiently to enable the great project to be completed. Dr. Stanley Barnes, who had already written a history of the medical school of the University of Birmingham, played a large part in bringing the matter to success and is well qualified to give an account of the combat—for combat it was—fought out in committee, in the daily papers, and even in public debate.

The story will chiefly appeal to the citizens of Birmingham, and others who read it may almost feel a little awkward as if they were looking in at a private quarrel. But everyone will be interested in the chapters giving practical advice on such matters as necessarily arise in the building of hospitals, and in the very brief but vivid character sketches of the men, well called protagonists, who played prominent parts in the conflict.

The advice on the choice of material for flooring and the remarks on the prevention of noise are useful, and the author's suggestion that steel girders should be insulated from the bricks by a layer of felt is original and perhaps worth trying; anything which would prevent the annoying sound of a water-flush from being heard at a distance would be a boon.

The short account of the chief characters enables us to realize the difficulties encountered. What can we think of a chairman who "would often open a committee meeting with a speech in parliamentary style lasting half an hour," and who on one occasion went on for 52 minutes and might have gone on longer if a necessary pause to take breath ("not for lack of a word," as the author emphasizes) had not allowed one of the members to interject a remark? When this orator one day met a generous donor who had just given £100,000 towards the hospital scheme, he remarked, "It almost makes me speechless," only to elicit the reply, "A miracle." The book is well, even luxuriously, produced, and is an object-lesson to the effect that public spirit, even outstanding public spirit, is sometimes difficult to guide along the right path.

ZACHARY COPE.

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FRUSTRATION IN THE HOSPITALS

In *The Times* last week Mr. A. H. Burfoot expressed in a letter the doubts and discontents of the many who have at heart the welfare of the hospitals of this country owned by the State and subject to an increasing degree of centralized control. "The London teaching hospital at which I am employed," he writes, "has a tradition of independence going back for more than two and a quarter centuries and a reputation that is world-wide. On the introduction of the National Health Service there were high hopes that tradition would be respected and reputation enhanced." He goes on to remind readers that a board of governors was appointed to manage the hospital on behalf of the Minister of Health "in accordance with regulations and such directions as may be given by the Minister." Mr. Burfoot reminds us again of the early assurance of the Ministry of Health that the Minister did not intend to use (perhaps abuse) his powers by controlling in detail the activities of boards of governors. Sir Russell Brain made a protest in a letter to the *Supplement* of November 22 last year about such detailed control. Admitting that there must be some control over the total consultant establishment, he doubted "whether this is best achieved by referring the decision in every individual case to Savile Row," where the Ministry is now housed. According to Mr. Burfoot no additional staff whatsoever—porter, domestic, nurse, doctor—may be engaged without Ministerial approval, which means, in fact, without the approval of a Civil Servant sitting in Savile Row: all this in spite of the fact that the budget has been approved. Mr. Burfoot gives the following example of the Ministry's capacity for pettifogging interference: "This board has now been told that it must seek the Minister's approval if, for example, it wishes to run an extension from the hospital's telephone switchboard to the accommodation of a resident employee required to be on call for night emergencies." This is the sort of thing that brings great discredit on the N.H.S. in the eyes of the world, especially in the eyes of the medical profession in other countries watching to see if the N.H.S. really will work. In a further letter to *The Times* Lord Knollys, with 25 years' experience of hospital management, draws attention to the frustration and delays resulting from the necessity to refer decisions to higher authority—to Savile Row. He points out that "the spending authority of those nominally managing the hospital group was so trivial that their effective decisions were limited to expenditure which was often little more than petty cash," so highly centralized has responsibility for finance become. Mr. J. W. D. Rowlandson, in a letter to *The Times* last Friday, said that the issue raised by Mr. Burfoot was worrying a large number of boards of governors. He points out—what must surely be obvious to the Ministry—that the present system of detailed control must defeat its very purpose, economy. The cost of the service must be increased, he suggests, by "the large number of officials necessary to determine whether in each of the 3,000 hospitals throughout the country an extra shorthand typist may be engaged or an additional telephone installed."

Members of boards of governors and of regional boards have far greater experience of hospital management than have the officials of the Ministry of Health. They are men of reputation in the world of business, medicine, and the law, and men with long records of public service. Much lip service has been paid in the past two or three years to the place and need for voluntary work in the N.H.S., and nowhere is this more necessary and valued than on the boards of governors of teaching hospitals and the regional hospital boards. Such men will not long tolerate the kind of futile and unintelligent interference to which *The Times* correspondence has drawn attention, and which they would not tolerate in their own undertakings, knowing that it leads to frustration, inefficiency, and waste of time and money. At the root of the matter there are two different attitudes of mind which seem at times to be irreconcilable. The Civil Servant commands respect because of his integrity, ability, and disinterested service to the community. But with this there appears to be a lack of trust in the capacity of other people to do their jobs properly, the attitude of a rather narrow-minded preparatory schoolmaster. You cannot run hospitals on a pigeonhole system. It was excessive centralization that brought down the General Board of Health almost exactly a hundred years ago, and the lesson was subsequently learnt that responsibility should be placed where it lies, on the individual local units, or, as it is fashionable to say these days, at the periphery. It seems that this lesson now has to be learnt once more. The energies of those on hospital boards should be bent on controlling their own affairs. The Civil Servants in Savile Row should be their servants, not their masters. The Minister and the Ministry should be content, we suggest, with providing the framework

of the service, with saying (helped by the Treasury) how much money in total is available, and leave the methods of its spending in the hands of those whose capabilities and training equip them to do it wisely. There is still a large body of disinterested and experienced men and women able and anxious to play their invaluable part in running the hospitals of this country. If their services are to be retained, and others are to be encouraged to succeed them, they must be allowed to exercise their full responsibility in an atmosphere of trust and free from frustration—otherwise the hospital service will degenerate to the ultimate harm of the patients it exists to care for.

THE METRIC SYSTEM

Rightly stigmatizing as archaic the apothecaries', avoirdupois, and imperial systems of weights and measures, Professor W. C. W. Nixon and Mr. T. D. Whittet, in an article at page 327, advocate their replacement by the metric system in medicine and pharmacy. So many are the advantages of the metric system, and so few the drawbacks of it, that only a conservatism akin to torpor could explain the survival much longer of the older systems. For to the difficulties of computation that the older systems provide, both within and between each other, must be added the confusion caused by having to work in several systems rather than one in the single sphere of medicine and pharmacy. The apothecaries' "drachm," for example, is homophonous with the avoirdupois "dram." But the drachm=60 grains and the dram=27.34375 grains; while the fluid drachm of water weighs 54.6875 grains. Again, the apothecaries' ounce=480 grains and the avoirdupois ounce=437.5 grains; yet the apothecaries' fluid ounce is equivalent not to 480 grains but to 437.5 grains. Such dangerous absurdities, as they have now become, have developed from modifications of exceedingly antique methods of weighing various commodities such as precious metals and wool. But surely the time has come to relegate them to nursery rhymes, there to join those quaint, possibly Celtic, terms of enumeration[1] now enshrined in the words "hickory, dickory, dock" and "eena, meena, mina, mo."

Nixon and Whittet make the important point that the medical profession cannot expect any help from the Government by legislation; indeed, not even the eventual abandonment of the archaic systems has been conceded as likely, though legislators have in the past often been more helpful, abolishing outmoded measures, modifying definitions, and establishing new standards to meet the demands of the community as they changed over the last 1,000 years. But the many modifications made were all to the old systems of weights and measures. The metric system has fared less well in Britain. Devised at the end of the 18th century in France, it was legally adopted in that country in 1795. Belgium, Holland, and Luxembourg followed suit in 1820, Spain and Italy in 1860 and 1861, and Germany and Portugal in 1872. Britain made its optional use legal in 1864.[2]

This was the cautious response of Palmerston's Government to the insistent advocacy of, among others, the distinguished mathematician Augustus de Morgan, who wanted to see the coinage decimalized first in order to accustom people in advance to the greater change of decimal weights and measures.[3] The matter was raised in the House of Commons in 1847, and the florin was issued in consequence. This movement, inspired initially in Britain by the publication in 1831 of a pamphlet by General Sir Charles W. Pasley, found many supporters in the succeeding 100 years but, apparently, not wide enough assent. When, therefore, the Government Committee on Weights and Measures was instructed early in 1949 to make recommendations for bringing legislation "into line with present-day requirements" hopes were raised that it would see the wisdom of introducing the metric system. Nor were they disappointed. In one of the most forthright Blue Books[4] to issue from a Government department the committee recommended that "the Government should take steps, in concert with the Commonwealth and the U.S.A., to abolish the imperial system of measurements in favour of the complete adoption of the metric system over a period of about twenty years." It also recommended the introduction of the metric system into medicine and pharmacy at the end of five years. Welcoming the report at the time,[5] we expressed the hope that the medical profession would investigate how soon its recommendations might be fulfilled. Since then it has not perhaps received the attention its importance deserves. But at least the Association of British Pharmaceutical Industry has taken an important step in the right direction, for it has recommended to its members that, from July 1 this year, "solids, liquid galenicals, and pharmaceutical chemicals should be sold in metric weights and measures (the liquids by volume)." This applies to drugs and galenicals supplied for dispensing, and not to pre-packed products for sale over the counter.

To follow this lead should not be too difficult for the medical profession even if, for a year or two, it entails a certain amount of extra thought. The last-

[1] Opie, I., and Opie, P., *Oxford Dictionary of Nursery Rhymes*. O.U.P. 1951.
[2] Sears, J. E., in *Chambers Encyclopaedia*, Vol. 9. London: G. Newnes. 1950.
[3] de Morgan, Sophia E., *Memoir of Augustus de Morgan*. London: Longmans, Green & Co. 1882.
[4] *Report of the Commission on Weights and Measures Legislation*. H.M.S.O. 1951.
[5] *British Medical Journal*, 1951, 1, 1195.

ing benefit would so outweigh the transient puzzling that medical men 20 years hence would look back with amazement at the reluctance of their seniors to institute the change. And there is much to be said for doing it overnight, as Nixon and Whittet suggest. The introduction in recent years of so many synthetic drugs prescribed in metric units makes the task relatively easy compared with what it would have been before, say, 1930, and itself provides some impetus to change. The slow acceptance of the system outside France would have dismayed its originators, who proposed to dedicate it "à tous les temps, à tous les peuples"—not without justification, as its universal adoption by scientists has shown.

THE TOLL OF FOG

The figures of the Registrar-General's office and the statement recently made in the House by the Minister of Health, Mr. Macleod, now enable us to form some idea of the immediate loss of life due to last December's disastrous fog. The Minister put the figure at 6,000, being the amount by which the 15,114 deaths in Greater London in the five weeks ending January 3, 1953, exceeded the number of deaths in the corresponding period last year. The Registrar-General's return for the week ending December 13, 1952, shows the deaths registered in the Administrative County of London as 2,484 in that one week, as against 945 in the previous week. If we take the figures for the same week for Greater London, including the Administrative County, we find 4,703 deaths against 2,062 in the previous week, while the average of the corresponding week of the last five years was 1,852. These figures indicate that 2,700 deaths within a few days may be attributed to the fog. Most would have been certified as pneumonia, bronchitis, or influenza. But there were no doubt also patients with chronic heart and lung disease whose end was hastened by exposure to the fog, and many of these would be included in the five weeks' figure of 6,000 given by the Minister. Most of the deaths were of people aged 45 and over. But the deaths of younger people do not show any notable increase in the weeks concerned except in the age group 4 weeks–1 year. It may be easier to get an emergency hospital bed for an acutely ill baby or child than for an elderly adult labelled bronchitis or even pneumonia, and good hospital treatment of a baby is apt to be more successful than of an elderly adult. An unusual feature noted in the treatment of several young babies affected by the fog was that aspiration of the alimentary canal yielded a surprising amount of filthy foggy material, and was beneficial. We await the full reports of such cases with interest. There is a danger that the obvious effects of the fog on babies and the elderly may divert attention from the damage possibly done to people in the middle years of life. The type of case worth studying is that of a stalwart London policeman of 35 who collapsed and was admitted to hospital only just in time to save his life by means of oxygen and treatment for shock. Full figures are not yet available of the number of cattle that perished in the disaster, but it is known that eleven had to be prematurely slaughtered at the Smithfield show, and over forty others were affected. Dogs were found to be the most susceptible animals in the lethal "smog" at Donora, U.S.A., in 1948.

These terrible disasters continue to recur, if at varying intervals, and further study of their causes and effects is needed. At the end of 1873 London had an exceptionally severe fog,[1] and an even more lethal one early in 1880,[2] when in the week ending February 7 the death rate in the metropolis was 896 per million inhabitants, as compared with 713 at the peak of the 1873 fog. The rate for the week ending December 13, 1952, was 745. Figures published for comparison in a report by Dr. J. A. Scott, medical officer of health to London County Council, show that in the worst week of the last great cholera epidemic—that of 1866—the London death rate was 876, and in the worst of the 1918 influenza pandemic it was 1,085. In December, 1930, the Meuse Valley Fog occurred in Belgium; 63 people perished and countless cattle had to be killed. The cause was said to be fluorides emitted from phosphate works, the air in the valley remaining stagnant for five days. The Donora fog killed nineteen people; their deaths were attributed to sulphur dioxide fumes from a zinc smelting works where ore containing much sulphur was roasted. The U.S.A. Government Report on the Donora smog episode is an impressive volume and should be studied by everyone investigating our fog of last December. It shows, for instance, that 42.7% of the Donora population of some 14,000 were in some way affected. All serious illness was over in a week except in 1.7% of the population. Post-mortem examinations, naked eye and microscopical, showed an acute toxic irritation, but no secondary infection. It was evident that pre-existing disease of the lungs or heart was a serious factor in determining susceptibility to smog. No eosinophilia was found. Here, as in the London fog, it was particularly noticeable that, once the fog had lifted, all symptoms cleared with remarkable rapidity, except in people suffering from chronic lung or heart disease. There is a need in the London outbreak for a full estimation of the size of the carbon particles (often "streaks" or "streams" were easily visible to the naked eye at Donora), which are said to penetrate further in a moist sulphurous-mist atmosphere. Post-mortem radiological findings may prove to be informative. The investigations now being made into the December fog deserve to be thorough, even if years must elapse before the remedies suggested by the analysis can be put into practice. Meanwhile a new device for detecting sulphur dioxide in the air has recently been reported from the U.S.A.[3] A small glass tube is filled with a vanadate-silica gel. This changes colour from red to green or blue in the presence of sulphur dioxide, which it can detect in concentrations down to 5 p.p.m. Another sulphur dioxide colour test has a periodate-silica base. These may have a useful part to play in the prevention of atmospheric pollution.

[1] *British Medical Journal*, 1873, **2**, 731.
[2] Ibid., 1880, **1**, 254.
[3] *Chemical Age*, November 1, 1952.

THE G.P. AND MASS RADIOGRAPHY

The part which the general practitioner can play in the control of tuberculosis is of the first importance, and in an article appearing elsewhere in this issue Drs. F. A. Nash and T. J. Lee and Mr. B. Benjamin describe how mass radiography might be brought to his aid. They found in an average London practice—and there is little reason to suppose that findings would be much different in other industrialized cities—that 2% of patients referred by general practitioners to a mass *x*-ray unit for the investigation of various "minor symptoms" not considered in themselves sufficient to justify referral to a chest physician were in fact suffering from active tuberculosis. This figure is many times higher than the average, now falling, of about three per thousand in the general fit population from which mass radiography units usually draw their examinees. Other medical directors who have encouraged general practitioners to send patients to their units have confirmed a high rate of infection among them. There will, however, be criticism of the suggestion that the units should concentrate solely on patients referred by general practitioners, for much useful preventive work now being done would cease.

There would be formidable practical difficulties in the way of any general scheme to encourage general practitioners to send patients with minor symptoms to a mass radiography unit. The radiologist would be the first to admit that his department could not cope with the extra volume of work; and the same applies to the chest physician, whose burden, already heavy, is increasing. But the latter would surely approve the principle of the scheme, for increased case-finding is one of the pillars in the control of tuberculosis. He might feel that work which was really in his province was being carried out by others not under his control, but this is unlikely provided that the mass radiography units avoided any tendency to become isolated chest clinics. The objection that such a scheme would tend to estrange the chest physician from the general practitioner is not justified. Those patients who in the general practitioner's opinion need investigation or treatment would still be referred direct to the chest physician. The mass radiography unit would act as a filter and send on to the clinic only those patients showing signs of abnormality. A general practitioner taking part in such a scheme would have to accept many normal reports for the sake of the very occasional discovery of active disease, but he might well feel that a negative report is a positive finding. He would of course have to guard against any temptation to put away his stethoscope, for the radiologist's report is still only an aid in coming to a final diagnosis. If such a scheme were put into operation it should be no more expensive than the present cost of mass radiography units, except for a slightly increased expenditure on large films—which would be called for at a later date in any case. The scheme would temporarily increase the notification rate and the demand for beds, but in subsequent years would be likely to result in a reduction in notifications, with a consequent smaller demand for beds.

In spite of these arguments many will feel that the restriction of a mass radiography unit's work to examination of patients referred by general practitioners is neither practicable nor advisable at the present time. After years of propaganda and the breaking down of resistance among employers, and to a lesser extent employees, the abandonment of the present scheme would be accepted, contrary to the evidence, as an admission of the failure of present mass radiography methods. The suggested change would exclude a large group of the population already used to mass radiography, and would put the industrial population at a higher risk. This would be a retrograde step and would certainly lead to many demands in doctors' surgeries for "a chit for *x* ray." But the results reported by Nash and his colleagues are sufficiently impressive to warrant an expansion of their work. There is here an opportunity for the more far-seeing regional boards to provide, possibly with the aid of the Medical Research Council, an additional static unit or two in suitable areas, so that further pilot investigations can be made. Future policy could then be based on the findings of these experimental units.

HEALTH SERVICE IN ANCIENT GREECE

Under this title Mr. A. G. Woodhead[1] has recently discussed what is known about the salaried medical service of classical Greece. Apparently each city elected one or more doctors by a free vote after the various candidates had spoken on their own behalf, and the chosen medical men then treated all the citizens without charge, if they so desired it. There were also private practitioners who could be consulted. But all citizens had to pay an annual health tax unless they were exempted from taxation because of some special service they had rendered the community. Appointments to the public service were for variable times, anything from one to twenty years, and seem to have been much sought after, though the salary was not large and was sometimes refused by the doctor, who presumably must have been already well-to-do. At this time doctors were regarded as skilled craftsmen, on a par with shipwrights. The public doctors probably treated slaves as well as free men, and certainly also treated foreigners without charge. A public doctor at Delphi in the third century B.C. was commended for the way tourists and visitors to the Oracle were cared for by him when they fell ill.

A State health service also existed in Egypt under the Ptolemies in the first centuries of our era. "A passage of Diodorus Siculus, for example, in mentioning that Egyptian doctors are paid by the Government, adds that they prescribe according to a written rule, set down by many doctors of the highest reputation. If they follow the treatment set down in the book, and yet cannot save their patient, they are free from all blame; but if they depart from the written instruction, and the patient dies, they are liable to a capital sentence." According to Aristotle, doctors could choose their own treatment if the official one had no effect after three days' trial.

[1] *Cambridge Historical Journal*, 1952, **10**, 235.

Mr. Woodhead also quotes an early nineteenth-century English traveller in Greece (E. Dodwell, there in 1801–6), who wrote that in his time "physicians in Greece, as well as in the small towns of Italy, are paid a yearly salary by the Government or public, and do not receive fees from their patients." So the State health service seems to have lingered on through many centuries.

These glimpses of the past are tantalizing; there is so much more we should like to know, but they are enough to show that "modern progress" is no new thing, even if to-day's setting and detail are different. Medical historians have for too long concentrated on recording the lives of outstanding clinicians of the centuries, and the evolution of medical theory. The life of the ordinary practitioner, and his actual medical practice, have been unduly neglected, though there are records available. The Greeks gave us a good deal of philosophy, a basis for medical ethics, and an example of clinical observation. If we care to inquire further we may find they have something still pertinent to offer in experience of medical organization.

THE DISABLED HOUSEWIFE

It is part of the practical work of rehabilitation departments to train patients in the use of orthopaedic braces and of the gadgets which help the seriously disabled to gain independence in the ordinary activities of day-to-day living. In addition vocational training is available for the disabled industrial worker and the handicapped child. One important person who has been almost entirely neglected in existing schemes of rehabilitation is the housewife. She, like the industrial worker, is subject to chronic illnesses and disabilities arising from rheumatic, cardiac, neurological, and other diseases, but, unlike him, cannot change her employment or retire, but has to rely on outside domestic help and day nurseries for her children. Resort to such methods of assistance is both uneconomical and unlikely to preserve a happy and well-run home. Cooksey[1] has recently described an alternative. In the physical medicine department at King's College Hospital the difficulties of the disabled housewife are now being assessed, and within the limits of her disability she is being taught to carry out domestic duties with the help of kitchen gadgets and other household aids. This application of the sheltered-workshop principle to the disabled housewife follows the example of workers in the United States. Their experience with these methods indicates that suitable training and inexpensive modifications to domestic appliances allow the majority of disabled housewives to return to full work. Thus the American Heart Association supplies to cardiac invalids a pamphlet[2] which guides them on how to carry out their domestic work within their cardiac reserve. Similarly, at the Bellevue Hospital, New York, there has existed for some time an experimental home-management clinic. King's has set a good example to other hospitals in Britain.

[1] *Ann. phys. Med.*, 1952, 1, 120.
[2] *The Heart of the Home*, issued by American Heart Association, New York.

THE TEACHING OF SOCIAL MEDICINE

The teaching of public health to undergraduates is on a firmer basis in the provincial medical schools than it is in London. All the provincial schools have departments of social or preventive medicine which undertake teaching and research. The solitary rather dismal exception is Oxford, which no longer has its institute or professor, and has to make do with a readership in social medicine. In contrast to the provinces, no London undergraduate clinical school has a separate department of social or preventive medicine, and only Guy's and the Royal Free Hospitals make calls on the staff of the London School of Hygiene for the teaching of public health. The Social and Preventive Medicine Committee of the Royal College of Physicians draws attention to these facts in a progress report,[1] and makes the guarded recommendation that other London medical schools should seriously consider following the example of Guy's and the Royal Free. The advisability of this can be judged from the committee's statement that "epidemiology in the wide sense does not appear to be treated systematically at any point in many London schools."

Though the London schools seem to have stood still since the committee last reported ten years ago,[2] progress in the provinces has been rapid. Direct instruction in social medicine now occupies 60 hours, compared with 37 in 1943. Another report from the Royal College of Physicians is on the subject of student health services (see p. 345), which some universities have linked with their departments of social or preventive medicine and found of value as an informal and indirect instrument of teaching. The curriculum too has been greatly expanded, and former public health courses have been replaced by "modernized courses in social and preventive medicine." Most medical officers of health looking at the brief classification of the "main topics dealt with by teaching departments of social medicine" would say that it was exactly these topics which comprised what they had always understood to be "public health." But even the Society of Medical Officers of Health has been impressed by a need for change and is considering the suggestion that its name should be changed to the Society of Preventive Medicine.

Agreement should be reached on terminology and also on the place that this subject, whatever it is called, should have in medical education. The dean of one medical school told the committee that social medicine cannot and should not be taught to the undergraduate student as a special subject. Preventive medicine, of course, cannot be ignored in teaching, for it is medicine at its best, and whatever may be thought of social medicine there is little doubt that with the world as it is it has come to stay. It is with the hope of throwing light on what is still an obscure corner of the medical curriculum that the World Medical Association has allotted an important place to social medicine in the First World Conference on Medical Education, which is to be held in London next August.

[1] *The Teaching of Social and Preventive Medicine, Progress Report*, January, 1953.
[2] *The Teaching of Social and Preventive Medicine, Interim Report*, 1943.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

CHEST PAIN

BY

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Chest pain is a very common symptom, and may arise from a variety of conditions in the chest and the chest wall. Sometimes the nature of the pain may strongly suggest the cause. Often, as in pain arising in the parietal pleura, although the source of the pain may be clear enough, the nature of the disease involving the pleura may be more difficult to elucidate. The exact significance of the pain may often be much less definite, and the question arises whether the pain is associated with any recognizable disease at all. When pain arises in association with some severe disease in the chest the need for treatment and further investigation is usually clear; by describing the main varieties and associated clinical features of such pain I shall try to indicate how the underlying cause may be suspected, so that treatment and investigation may be helpfully directed. My other main purpose is to describe some of the types of chest pain not so clearly related to disease in the chest, and to consider when further investigation, in particular radiography, is called for in patients with this sort of pain.

Cardiovascular Disease

Chest pain associated with cardiovascular disease has already been discussed in this series by Dr. A. Rae Gilchrist (see *British Medical Journal*, 1951, 1, 874, 937). It will be sufficient here to describe briefly the pain associated with a few important kinds of cardiovascular disease. The most important type of heart pain is that which occurs with coronary insufficiency and is nearly always felt behind the sternum. It can be of any grade of severity, and may or may not radiate to the arms, jaws, neck, or back. It is almost invariably at first the result of effort and usually paroxysmal, the term "angina of effort" being used to describe it. More prolonged pain of this type is most commonly due to myocardial infarction from occlusion of one of the main coronary arteries or branches.

There are less common varieties of chest pain of cardiovascular origin. Dissecting aneurysm of the aorta usually produces an excruciating pain behind the sternum or in the back, and often radiating down the legs. The pain may suggest that coronary occlusion has occurred, but it may sometimes be possible to arrive at the correct diagnosis if evidence of early blocking of peripheral arteries can be established. An aortic aneurysm may produce a severe aching type of pain in the upper chest owing to the pressure of the growing aneurysm on the sternum, ribs, and other surrounding structures. Pain due to acute pericarditis is not common. When it occurs it may be felt near the sternum and is usually made worse by inspiration, which may help to distinguish it from the pain of myocardial infarction. In all of these varieties of pain there is usually a good deal of other evidence to connect them with severe cardiovascular disease. A large number of patients, as is well known, complain of pain over the heart, by which they usually mean pain over the left nipple region. This sort of pain is not due to heart disease and is considered below with the less definite types of chest-wall pain.

Oesophageal Pain

Lesions of the oesophagus may cause pain which is usually felt behind the sternum but sometimes in the back of the chest. Peptic ulceration of the lower end of the oesophagus is usually associated with sliding hernia of the stomach into the mediastinum. It occurs mainly in the age group 50–70 years, and is almost equally frequent in men and women. Symptoms of the hernia itself are epigastric fullness and discomfort after meals, but if oesophagitis occurs owing to regurgitation of acid gastric juice through the incompetent sphincter, then intense burning pain may be felt behind the lower end of the sternum. This may radiate to the back, when it usually indicates spread of the inflammation from the submucosa to the deeper layers of the oesophagus and the mediastinum. The pain is often more severe when the patient bends forward or lies down. In the condition called "cardiospasm," or "achalasia of the cardia," pain is not a usual symptom. When felt, it is a painful sense of constriction behind the lower sternum which follows the taking of food. In carcinoma of the lower end of the oesophagus or cardia of the stomach pain is not an important symptom. It may be felt in the back in cases of mediastinal involvement. In general, the association of alimentary symptoms such as dysphagia, which may be intermittent, and the regurgitation of food will suggest the oesophageal origin of these types of pain.

Sometimes, however, it may be difficult to decide whether pain felt behind the lower sternum is of cardiac or oesophageal origin. Indeed, it is possible that herniation of the stomach through the oesophageal hiatus of the diaphragm may precipitate anginal pain when the coronary arteries are sclerotic. Moreover, it has recently been shown that a number of patients with pain of cardiac type, in whom adequate electrocardiograms show no abnormality, have an abnormal oesophageal mechanism, described as oesophageal arrhythmia. It is therefore well worth directing investigation to the oesophagus when the cardiac origin of pain behind the sternum cannot be firmly established.

Pleural Pain

The visceral pleura and the lung itself are devoid of pain sense. When diseases involving the lungs and pleural cavity are associated with pain, it arises from the parietal pleura. The mechanism of the production of this pain is not completely understood, but it is probable that it is due to stretching of the parietal pleura, either mechanically or by an inflammatory process, rather than to the rubbing of inflamed pleural surfaces. So far as the costal pleura is concerned, pain is usually localized on the chest wall fairly exactly over the area of the pleura involved. Nevertheless, certain generalizations about the site of pain arising in the pleura may be made. Involvement of the apical pleura is rarely sharply painful, but produces a sense of soreness or pain in the shoulder which may be thought to be due to shoulder-joint disease. Pleural pain is most commonly felt in the nipple or axillary regions, but may spread, or be confined, to the region of the angle of the scapula. It is commonly severe, and every movement and inspiratory effort intensifies its lancinating quality. If the diaphragmatic area is involved the pain may be felt low down in the back, in the abdomen, or in the neck and shoulder. Diaphragmatic pain is discussed below.

Tuberculous Pleurisy.—This is the commonest cause of pleural pain in adolescents and young adults, and also occurs often enough at other ages. It arises usually in the absence of clinical or radiological evidence of pulmonary tuberculosis, but does occur in established cases. Often the onset

of the pain is described as sudden, but on questioning the patient it commonly becomes clear that there has been a preceding period of vague ill-health. In most cases the first definite intimation of trouble is the pain. This is accompanied by fever, and because of the pain the breathing is rapid and shallow. Clinical examination will show diminution of rib movement on the affected side, and the deciding physical sign is the friction rub. Sometimes the symptoms and signs are much less striking. When a young person, perhaps vaguely unwell, presents himself with rather indefinite pain in his axilla or below his scapula, and on physical and even radiological examination nothing abnormal is found, it is often wise to see him repeatedly at short intervals, for the signs of pleurisy may be slow to appear. In tuberculous pleurisy this dry stage is usually but not invariably followed by the stage of effusion. When this occurs the pain disappears entirely or at most leaves a sensation of soreness over the chest wall. A further point should be mentioned about pain in tuberculous pleurisy. It is very common for patients to complain of pain over the lower part of the chest wall for months or even years after the pleurisy has cleared up and the effusion has disappeared. This may be more severe and prolonged when there is evidence of residual pleural fibrosis, but it does occur in the absence of this. It is not usually severe and very often responds to reassurance.

Pulmonary Tuberculosis.—Patients with pulmonary tuberculosis not infrequently complain of persistent pain in the chest wall in the neighbourhood of the site of the lung lesion. While it is unusual to hear a pleural friction rub in these circumstances, there can be little doubt that the pain often arises in the pleura. At any rate there seems to be an association between the presence of this sort of pain and the presence of pleural adhesions, as can be shown when treatment with artificial pneumothorax is attempted.

Pneumonia.—The onset of pneumonia, whether of the acute specific type or an aspiration pneumonia, is very often associated with pleural pain. This may be very severe and a friction rub may be heard. Sometimes it may be extremely difficult to decide whether a tuberculous pleurisy or a pneumonia is beginning. Usually in a pneumonia the physical signs of consolidation and the presence of sputum indicate the correct diagnosis, whereas in tuberculous pleurisy effusion develops quite rapidly. However, the difficulty of deciding whether an effusion has developed in association with a pneumonic process or has resulted from a tuberculous pleurisy may be very great and will be considered further in next week's article on pleural effusion.

Chronic Bronchitis.—Patients with chronic bronchitis not infrequently, and especially in the winter, get episodes of pleural pain associated with increase in cough and sputum, and sometimes with fever. These episodes are mostly due to the development of small areas of aspiration pneumonia which arise by the blocking of small bronchi by sputum and infection of the atelectatic lung beyond the block. While this process may occasionally lead to suppuration in the lung, the condition usually clears up quite quickly with the expectoration of the blocking material. In bronchiectatic patients rather similar episodes occur and are due to spread of infection from the dilated bronchi into the surrounding lung.

Bronchial Carcinoma.—Pain may arise in several ways in association with bronchial carcinoma. When a carcinoma blocks a bronchus a pneumonia or infected atelectasis may develop in the lung distal to the block. The pleura over the involved lung may be inflamed and typical pleural pain arise, often followed by effusion. Secondary deposits of growth on the pleura commonly result in effusion also, but not so frequently in pain, although this does sometimes occur before the fluid accumulates. Extension of the growth to the chest wall may produce very severe pain by involvement of nerves and ribs. In all these circumstances the illness of the patient and the considerable abnormalities detected on clinical examination will nearly always point to the urgent need for further investigation of the chest. Sometimes the chest-wall pain is much more vague and indefinite and not associated with abnormal findings on physical examination. This is referred to below in connexion with the general investigation of this sort of pain. The early diagnosis of bronchial carcinoma was the subject of an article by Mr. R. C. Brock earlier in this series (see *British Medical Journal*, 1950, **1**, 116).

Pulmonary Embolism and Infarction.—Pulmonary infarction is commonly associated with pleural pain on the affected side. Here there are certain features which will suggest the correct diagnosis. Apart from post-operative surgical and obstetrical patients, this condition most commonly occurs in those with heart disease, in those with saphenous varicosities or thrombophlebitis, and in elderly patients confined to bed. In these circumstances phlebothrombosis of the leg veins is apt to occur, and emboli may break loose and reach the pulmonary circulation. The symptoms of pulmonary embolism may be so slight as to be unnoticed, may consist of transient breathlessness and tightness in the chest, or, at the other extreme, a state of severe shock may be produced. The massive emboli which result in death are most commonly seen in surgical and obstetrical patients. Infarction by no means always follows embolism, but when it does pain is a prominent symptom and is usually present by the second day of the illness. A friction rub is not commonly heard, and signs of phlebothrombosis in the leg are often absent. The most useful diagnostic features are the type of patient, the sequence of events, the fact that the onset of the pain is usually quite abrupt, and the common recurrence of attacks as further emboli reach the lungs. In addition, persistent haemoptysis occurs in rather less than half of these patients, and when present is a great diagnostic help.

Bornholm Disease.—This is a benign condition, almost certainly a virus infection, which is most easily recognized when it occurs in small epidemics, though sporadic cases probably also occur. Pain is the most striking feature, and, although it may not truly arise in the pleura, it is probably best described in this section. It is felt commonly in the region of the costal margin or the upper abdomen, and also sometimes in the shoulder, and becomes worse on deep breathing, coughing, yawning, laughing, and also on movement. Muscular pain and tenderness elsewhere over the chest is a not infrequent accompaniment. The patient is febrile, and a coarse pleural friction rub is sometimes heard. There is often some abdominal tenderness, commonly just below the costal margin. In some patients the symptoms may be mild, with pain only on deep respiration, and associated with slight malaise only. In others the pain may be severe, with high fever and perhaps abdominal rigidity. The duration of the pain is usually a few days, but it may disappear and recur. The importance of recognizing this condition lies mainly in distinguishing it from more serious causes of similar pain. If a number of cases occur together, this is very suggestive of Bornholm disease. It can usually be distinguished from tuberculous pleurisy by its relatively transient nature and by the complete absence of effusion. When abdominal pain and tenderness are prominent features acute appendicitis or other acute abdominal emergencies may be confused with it. The fever at the onset, the normal leucocyte count, and the fact that the pain from the beginning is worse on deep breathing should suggest the correct diagnosis, provided this is kept in mind.

Diaphragmatic Pain.—Pain arising from the pleura over the diaphragm presents certain peculiar features, some of which have already been mentioned. If it arises from the central part of the diaphragm, which is supplied by the phrenic nerve, then it may be felt at the shoulder or along the border of the trapezius muscle. If it arises from the periphery of the diaphragm, which is supplied by the lower intercostal nerves, it may be felt over the lower chest, the lumbar region, or the abdomen. Thus patients who have any of the intrathoracic conditions associated with pleural pain, and in whom the condition affects only the diaphragmatic region and does not impinge on the costal pleura, may complain of pain remote from the chest. The most danger-

ous instance of this is when the abdominal localization of the pain simulates acute appendicitis or other acute abdominal condition. Usually the presence of respiratory symptoms, such as painful cough or hurried painful breathing, or the presence of some abnormal signs at the base of the chest, will indicate the true source of the pain. Exceptionally, there may be no indication at first that the respiratory system is involved, and it may require great surgical judgment to decide that there is no abdominal emergency.

Spontaneous Pneumothorax.—The onset of a spontaneous pneumothorax is sudden in approximately three-quarters of the diagnosed cases. The patient is seized with pain in the side, usually felt over most of the chest wall but sometimes worst at the costal margin. With the onset of the pain difficulty in breathing develops. In some cases extreme dyspnoea occurs and the patient may become severely shocked. However, these symptoms vary greatly in severity. In cases with an insidious onset a pneumothorax may develop with few symptoms to draw attention to it. As the air accumulates, difficulty in breathing develops, and even if distinct pain does not occur a feeling of oppression in the chest is common. Patients with spontaneous pneumothorax are usually afebrile, which helps to distinguish them from those with inflammatory processes involving the pleura. The useful physical findings are the resonant percussion note with absent breath sounds and no added sounds. The features which most suggest the diagnosis are the pain, usually widely felt over the chest wall, and the developing dyspnoea in the absence of signs of effusion or pneumonia.

Other Varieties of Chest Pain

A raw feeling not always amounting to pain is quite commonly felt over the upper part of the sternum by patients with tracheitis. Occasionally this is severe enough to be the main complaint, but the association with an upper respiratory infection which progressed to produce a painful cough will usually make the diagnosis clear.

Pain localized to one or sometimes two costal cartilages and associated with acute tenderness of the cartilage may be a very distressing complaint. The exact site of the pain and tenderness is characteristic enough to make this a fairly easily recognizable type of pain, which is believed to be due to costal chondritis.

Patients who have a cough, and not always a very severe one, from whatever cause, sometimes complain of sudden severe pain while coughing, usually in the lower chest. They may state that they felt as though one of their ribs had cracked. The pain may be worse on breathing and this may suggest a pleural origin. However, localized tenderness over a rib and carefully directed radiography may demonstrate a rib fracture—the "cough fracture"—as the cause. Sometimes the radiological demonstration may be delayed until the formation of callus shows the site of the fracture.

Localized pain over a rib, particularly in a middle-aged or elderly man, must suggest the possibility of secondary deposits of carcinoma. In this connexion it should be mentioned that pain down an arm, especially the medial border, may be due to the involvement of nerve roots by an apical carcinoma in the lung. Again, particularly in a middle-aged or elderly man, persistent pain of this sort should suggest the advisability of further investigation of the chest.

Pain in the distribution of a thoracic nerve may be caused by the pressure of a tumour—for example, a neurofibroma may develop in the intervertebral foramen and compress the nerve. Pain of this sort may also be associated with spondylitis and with spinal caries. Herpes zoster produces pain of this type, but in this condition the diagnosis becomes clear with the development of the eruption.

Pain which may be very severe may arise in the muscles of the chest wall. The source of such severe pain is usually definite enough because of the tenderness of the affected muscles and the increase in pain when they are used. There may also be a history of recurrent attacks of similar pain, and other groups of muscles may be affected at the same time. Besides this sort of muscular pain a large number of patients complain of relatively minor pains or aches situated in various parts of the chest wall, many of which probably arise in muscles. The commoner sites for these more vague pains are the pectoral regions and the areas medial to and below the scapulae. They are often brought on by an unaccustomed use of the arm—for example, a new job involving an arm movement not previously used. They are also often associated with anxiety about the presence of chest disease, and may be much relieved by reassurance after appropriate examination and investigation. Precordial aching is a common symptom of the effort syndrome and allied anxiety states. It occurs as a dull ache in the region of the left breast. Tenderness of the skin and muscle usually accompanies it and is an important clue to its proper interpretation, since pain due to coronary insufficiency, besides being almost always sternal in its situation, is not accompanied by superficial tenderness of the chest wall.

Radiography in Chest Pain

As was pointed out at the beginning of this article, in many patients who present themselves with pain in the chest the crucial problem from the doctor's point of view is whether, after physical examination has been carried out, further investigation of the chest is called for. This will usually mean the taking of a chest radiograph as the next step. In the sorts of pain described as being likely to be associated with various forms of intrathoracic disease this decision may not be difficult. Thus in patients who develop pleural effusion or who have pneumonia radiography will be used appropriately in the management of the condition.

Patients in whom the character of the pain suggests myocardial infarction will be suitably treated and future investigation directed to the cardiovascular system.

The problem arises most frequently in those patients who complain of the more vague and indefinite forms of chest-wall pain. These pains are often associated with some tenderness of the muscles, and, apart from this, no abnormal signs are found over the chest. There is no doubt that both pulmonary tuberculosis and bronchial carcinoma are found in patients who present no more than this sort of symptom. The problem is to select the few who have serious pulmonary disease from the many more who do not. Some patients, in whom the pain is transient or clearly associated with some unaccustomed muscular exertion and ceases as the patient becomes used to or abandons the particular effort, need not be further investigated. For the rest there is no simple solution, and when this sort of pain persists for two to three weeks it will usually be advisable to have a chest radiograph taken. An additional reason for this is that these pains are often expressions of anxiety about chest disease and are often relieved after what is felt to be adequate investigation. In many of these patients physical examination followed by a postero-anterior radiograph is all the investigation required, and this would seem to be one of the more appropriate ways in which the general practitioner could use the mass miniature radiography service.

Next Refresher Course Article.—"Pleural Effusion," by Dr. Howard Nicholson.

Experiments on rats have led to a belief that a bad diet may play a part in causing addiction to alcohol. In these experiments rats had a choice of water or alcohol to drink, and it was found that those on a good diet preferred water, while those which were inadequately fed consistently chose alcohol. At first sight this seems conclusive enough, but new tests done by two Yale scientists put the rats' behaviour in a different perspective. They offered the rats three drinks to choose from—water, alcohol, and sugar solution. The hungry rats immediately abandoned their alcoholic habits and took to the sugar solution. They only returned to the alcohol when the sugar solution was exhausted (*New York Times*, January 25).

THE METRIC SYSTEM IN MEDICINE AND PHARMACY

BY

W. C. W. NIXON, M.D., F.R.C.S., F.R.C.O.G.

AND

T. D. WHITTET, B.Sc., Ph.C., A.R.I.C.

The replacement of the archaic apothecaries', avoirdupois, and imperial systems of weights and measures by the metric system has long been advocated by progressive doctors and pharmacists. As long ago as 1826 Andrew Duncan[1] pointed out the inconvenience of imperial and apothecaries' measures and suggested the use of decimal multiples of the grain. An annotation on his letter in the *Lancet*[2] approved this suggestion in principle but recommended that, "instead of adopting an alteration of weights for pharmacy, as proposed in this letter, it would be more advisable to wait a little, *until the Government shall ordain the decimal proportions of weights and measures to be generally used, which we anticipate to see done in a few years*" (our italics).

In 1944 one of us (W. C. W. N.)[3] advocated in this *Journal* a change to the metric system. This gave rise to considerable correspondence,[4-10] all in favour of the proposed change. Following this metric equivalents were introduced into all articles published in the *British Medical Journal*.

The British Pharmacopoeia Commission has advocated that the medical and pharmaceutical professions should use the metric system exclusively, and since 1914 all the formulae of the *Pharmacopoeia* have been expressed in the metric system, while doses have been given in both metric and imperial. It is interesting to note that in the preface to the 1914 pharmacopoeia the following statement occurs: "*The metric system has also been employed for the specification of doses, in the expectation that in the near future the system will be generally adopted by British prescribers*" (our italics). The *British Pharmaceutical Codex* employs both imperial and metric systems side by side in all its formulae, monographs, and doses.

Archaic Systems

From the teaching point of view, we regard it as a retrograde step that on entering his clinical course the student has to be taught the archaic systems of weights and measures. During his preclinical pharmacology course he is accustomed to using drugs in terms of the metric system and has also used that system in his other scientific subjects. He must therefore gain the impression from the old-fashioned systems that clinical medicine and pharmacy have lagged behind the other sciences and still cling to outmoded methods. Since the war English textbooks of medicine and pharmacy are being used to an increasing extent in many Continental countries; therefore it is most important that the metric system should be used in such publications.

As Bodenham has pointed out,[11] it is the custom for all new drugs to be measured for dosage in terms of the metric system, and hence the proportion of commonly used drugs measured in the apothecaries' system is steadily decreasing. This trend has brought the farcical state of affairs that older analgesics, such as morphine and diamorphine, are almost invariably prescribed in fractions of a grain, whereas the very similar newer synthetic analgesics, such as pethidine and methadone (amidone), are always prescribed in milligrammes. Many similar examples could be quoted. Since most hypodermic syringes are graduated in the metric system it is not uncommon to find mixtures of the two systems used for injections—for example, atropine sulphate 1/100 gr. in 1 ml.

This multiplicity of systems leads to confusion and serious or even fatal errors, and there seems little excuse for retaining the obsolete apothecaries' and imperial systems.

Government Report

Some years ago a Committee on Weights and Measures Legislation was set up by the Board of Trade with the following terms of reference: "To review the existing weights and measures legislation and other legislation containing provisions affecting weights and measures and administration thereof, and to make recommendations for bringing these into line with present-day requirements." This committee, after hearing evidence from the British Medical Association, the Pharmaceutical Society, and other interested bodies, issued its report in 1951.[12]

The recommendations were (1) that the apothecaries', troy, and pennyweight systems of measurement should be abolished after five years, and the trades and professions at present using them should adopt the metric system in their place; (2) that the Board of Trade should define suitable tolerances for metric weights and measures (the British Standards Institute is at present drawing up standards for metric measures); and (3) that the Government should take steps in concert with the Commonwealth and the U.S.A. to abolish the imperial system of measurement over a period of about 20 years.

In its evidence to this committee the British Medical Association stated that the medical profession is probably in favour of using the metric system, but that abolition of the apothecaries' system would cause some hardship to the middle and older generation of doctors. The Pharmaceutical Society favours the change, provided that doctors cooperate in writing all their prescriptions in the metric system and do not leave it to the pharmacist to translate apothecaries'-system prescriptions into the metric system.

In the early part of 1952 the Association of British Pharmaceutical Industry made an important decision which will have the effect of implementing some of the recommendations of the Board of Trade Committee. The association decided that, from early 1953, all galenicals and pharmaceuticals should be sold on the metric system in pharmacy. This has the support of the Pharmaceutical Society and the Guild of Public Pharmacists.

The Association of British Pharmaceutical Industry has also approached the Glass Manufacturers' Federation with a view to the standardization of a range of bottles suitable for metric quantities from 25 ml. up to 2½ litres. If this can be arranged it would facilitate a transition to the metric system for medicines.

Government Reluctance

In the House of Commons on May 10, 1951, the then President of the Board of Trade, giving a written answer to a question, said that among the recommendations of the Board of Trade Committee were some which the Government could not accept, at least for immediate implementation. The proposal that the Government should take steps towards the eventual complete adoption of the metric system in this country clearly raised most important issues which could not be determined without lengthy and most serious consideration. On November 11, 1952, the President of the Board of Trade stated that the Government was not prepared to proceed with the recommendation for the eventual abandonment of the imperial for the metric system of weights and measures.

These statements by two different Governments make it clear that we cannot expect the adoption of the metric system to come by legislation, and if the professions wish it they must make their own decision. The reluctance of the Governments to take such a step is probably because of the

expense and inconvenience involved in the recalibration of machine tools and precision instruments. These factors would not affect medicine and pharmacy.

The main objections to the metric system are the fear of a misplaced decimal point leading to gross overdosage and the difficulty of memorizing doses in fractions of a gramme. Both of these disadvantages could be overcome by the use of milligrammes, centigrammes, etc., as has been advocated by Beard.[8] On the whole the few disadvantages of the metric system would be greatly outweighed by the abolition of the present confusion and general simplification of measurements which would result from its exclusive adoption in medicine and pharmacy.

Overnight Change

We realize that the change we advocate would mean a certain amount of hardship to those who had to change their prescribing habits with the older drugs, but we consider the eventual result would justify this. As Marsh[6] has pointed out, the change would cause no more disturbance than the introduction of a new *British Pharmacopoeia* or *British Pharmaceutical Codex*.

On the whole we favour an "overnight" change (after due notice had been given) rather than the gradual change suggested by the Board of Trade Committee. We are impressed by the letter of Lambert Rogers[9] giving an analogy with an overnight change of nautical helm orders some years ago. Critics had predicted many dire consequences of this sudden change, whereas in practice it took place without mishap or confusion. We urge that the General Medical Council, the British Medical Association, the Pharmaceutical Society, and the universities and other examining bodies should take action to implement this change, otherwise the present confusion is likely to continue indefinitely and we shall be the sole country out of step with the rest of the world, just as we are one of the few remaining who drive on the left of the road and call surgeons "Mr."

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6 Doutnwaite, A. H., ibid., 1944, 2, 478.
7 Rushbrook, S. A. W., ibid., 1944, 2, 478.
8 Beard, T. C., ibid., 1944, 2, 638.
9 Rogers, L., ibid., 1944, 2, 639.
10 Horsford, J., ibid., 1944, 2, 738.
11 Bodenham, D. C., ibid., 1952, 1, 819.
12 Ibid., 1951, 1, 1195.

Leander Starr Jameson, remembered as the leader of the famous "Jameson Raid," was born on February 9, 1853. He studied medicine, and qualified from University College Hospital, London, in 1875. After a short time in practice in this country he emigrated to Kimberley, in South Africa, where he soon built up a great reputation. As a result of his friendship with Cecil Rhodes he undertook three fruitful missions to the Matabele chief Lobengula, from whom Rhodes had obtained concessions of mineral rights. Jameson later became administrator of Mashonaland, and by 1894 had reached the zenith of his fame. About this time the discontent of the "Uitlanders" with the Transvaal Government was coming to a head, and plans were being made for its forcible overthrow. Jameson undertook the task of raising a mounted force in Rhodesia and holding it in readiness for any eventuality. In defiance of wiser counsels he entered on his historic "Raid" by crossing the Transvaal border on December 29, 1895. His force was soon defeated by the Boers, and Jameson was handed over to the British authorities, being eventually sentenced in London to 15 months' imprisonment. He was released for health reasons and soon came to the fore again, becoming Prime Minister of Cape Colony in 1904 and the foremost figure in South African politics. He worked in amity with Botha to achieve the Union. In 1911 a baronetcy was conferred on him. Continued ill-health led him to return to England, where he died on November 26, 1917.

Nova et Vetera

ARCHITECT OF PUBLIC HEALTH

The Life and Times of Edwin Chadwick. By Professor S. E. Finer. (Pp. 555. £2 2s.) London: Methuen and Co. 1952.

It has often been regretted that, although Edwin Chadwick was the great architect of social and public health administration in the first half of the nineteenth century, no full-scale biography of this remarkable man has been written. His admirer, Benjamin Ward Richardson, in editing in 1887 a selection of Chadwick's papers entitled *The Health of Nations*, prefaced the book by a short life in which Chadwick himself took great personal interest, and brief lives have also been written by Marston and others; but these studies obviously omit much in the telling. This deficiency has now been supplied by Professor Finer's full and scholarly biography.

The author traces the stages of Chadwick's meteoric career; first, the attorney's clerk and barrister, and the formative years when he sat at the feet of Jeremy Bentham.

"The influence of legal training and, in particular, the legal models of Bentham and the French codes fostered a mental attitude which he never shook off and which determined his approach to all social problems he afterwards investigated."

Secondly, the arbiter, motive power, and director of the Poor Law Commission, where his draconian methods, satirized in *Oliver Twist*, led to his dismissal in 1847.

But his famous *General Report on the Sanitary Condition of the Labouring Population of Great Britain*, the opening cannonade of a century of public health reform, had appeared in 1842, and a Royal Commission was appointed which confirmed Chadwick's indictment of the terrible conditions of social degradation and disease which prevailed in this country.

The Public Health Act of 1848 was passed, and Chadwick entered on the third stage of his career as the moving spirit of the General Board of Health, being associated as Commissioner with the First Commissioner of Works (*ex officio*) and Lord Ashley. Professor Finer shows how Chadwick's intolerance and fanaticism, qualities fatal to human relations, defeated the very ends which he had in view. "Unable to bend, he was made to be broken." As he disdained compromise and ignored opposition in his zeal for public-health reform in a hurry, public opinion denounced him, and to placate it Lord Palmerston persuaded him to resign on a pension in 1854. The rest of Chadwick's long life was an anticlimax, though he continued to advocate public-health reform incessantly and witnessed its triumphs. In the year before his death he received belated recognition by the bestowal of the K.C.B.

If at times the author dwells too much on "old unhappy far-off things and battles long ago," he has on the whole faithfully depicted the shadows as well as the highlights of Chadwick's character. The self-arrogant Chadwick was ungrateful to Southwood Smith, Neil Arnott, Kay, and others. Although these medical pioneers had brought to his notice the sanitary crimes he assailed and had instructed him in the means for combating them, he looked on doctors "as necessary evils and not very likely to last."

Nevertheless, Chadwick was a great man. He re-forged four distinct social services and reformed the entire system of local government. When his colleagues were unmoved by injustice, poverty, dirt, and disease, Chadwick assailed these evils and prodded the apathetic into activity. That is why the Prince Consort, Lord Shaftesbury, Sir John Simon, and other enlightened men of those days esteemed his work, and why medicine and public health reap to-day the reward of his labours, so admirably set forth in this authoritative biography.

ARTHUR S. MACNALTY.

Reports of Societies

HOMOLOGOUS TISSUE TRANSPLANTATION

The Medical Society of London held a discussion on "The Present Status and Future Prospects of Homologous Tissue Transplantation" on January 26. With the President, Dr. CUTHBERT DUKES, in the chair, Mr. W. J. DEMPSTER began by saying he would confine his contribution to the homografting of skin and the homotransplantation of kidneys, studied in animal experiments. Skin grafting was technically straightforward and the results could be observed directly. With the kidney it was easy both to provide a satisfactory blood supply and to study function by collecting the urine the kidney made. Scientific understanding of the nature of the disintegration of tissue homografts began with the recent work of Professor P. B. Medawar. He showed that the first time skin from rabbit A was grafted to rabbit B the graft survived about 10 days. The second time skin was grafted from A to B survival time was reduced to four days. But skin from a third rabbit, C, grafted into B at the same time, survived 10 days like the first graft of A. This suggested that B developed an actively acquired immunity, which was individual-specific to the skin of A. If, instead of the first skin grafting, leucocytes from A were injected intradermally into B, and then skin was grafted from A to B, although this was the first skin graft, it disintegrated at the rate usually associated with the disintegration of a second skin graft. This meant that the leucocytes had sensitized B to A's skin. Evidently the rabbit was already immunized, and the actively acquired immunity, though individual-specific, was not tissue-specific. Whole-body irradiation was known to delay the antibody response to bacterial antigens if it was given a few hours before the first antigenic injection. Mr. Dempster had similarly increased the survival time of skin grafts by prior whole-body irradiation of the recipient, which was further evidence that homologous skin grafts failed because of the development of antibodies.

Kidney Transplants

He said that for kidney experiments he and his colleagues used greyhounds, as this was the only breed which did not commonly suffer from a spirochaetal nephritis. The donated kidney was grafted into the neck, renal artery anastomosed with carotid artery and renal vein to external jugular vein; within ten minutes of acquiring its new blood supply the kidney started to secrete. Detailed study of controls, in which the kidney was transferred from the belly to the neck of the same dog, showed the importance of taking out the kidney quickly if it was not to become anuric through severe renal arteriospasm. With good technique less than 5% of kidneys suffered this fate. The auto-transplanted kidney, though it had lost its concentrating power, would keep the animal alive for at least 15 months.

The homologous transplanted kidney behaved at first in the same way. But at a varying time up to three weeks it suddenly became anuric, and arteriograms showed severe intrarenal arterial spasm. Biopsy specimens taken at intervals after transplantation showed histological changes from about the third day. Mr. Dempster interpreted them as the transplanted kidney's response to its host's circulating plasma proteins, which of course were "foreign" to it.

A second kidney transplanted from dog A to dog B behaved quite differently. It functioned at the most for a few hours. When anuria set in arteriograms revealed widespread spasm. At the same time the kidney was swollen and biopsy everywhere showed glomerular dilatation and tubular death, with deposits of fibrinoid material in the intercapillary space of the glomerular tufts. The picture was very like that after the injection of nephrotoxic sera, and suggested a severe antigen–antibody reaction. Cortisone did not affect the ultimate survival of transplanted kidneys, although it certainly did increase the blood flow through them up to ten times even when such kidneys became anuric. Thus the immediate outlook for successful kidney transplantation was very poor.

Corneal Grafting

Mr. B. W. RYCROFT discussed corneal grafting. The idea was as old as the Society, but up to the beginning of this century visual results had been disappointing owing to infection and heteroplasty. However, too much emphasis should not be placed on heteroplasty, as it had recently been shown that heteroplastic grafts of cornea from cat to rabbit were possible: infection probably ruined many early cases. The general view was that a corneal graft was a scaffold graft rather than a true graft: cells were replaced by the host, but membranes remained. A microscopic section was shown of a human homograft which had been transparent for three years after operation.

Different surgeons used different indications, and criteria of success varied and were difficult to compare. Some judged a graft on clarity; others on visual improvement. In his own cases about 60% had visual improvement after a split corneal graft and 30 to 40% after a full-thickness graft. There were many causes of failure in graft surgery, but only two were pertinent to the present discussion—namely, vascularization and oedema of the graft. Vascularization was not the menace it had been, owing to the use of local β-radiation of host and donor; cortisone was also of great value in inhibiting newly formed blood vessels, but it should not be used immediately after operation. Oedema was still a problem, especially that which occurred about the tenth to twenty-first day. A second graft operation on an oedematous cornea could and often did remain clear, showing that there was possibly an antigen–antibody reaction.

The most suitable eye for donor purposes was that of an aged person who had died a natural death; eyes from stillborn infants were too soft and tended to react with vascularization. The Corneal Grafting Act of 1952 had become law and already eyes from bequest had increased. It looked as if the donor problem was going to be solved.

Other Types of Graft

Mr. A. L. SCHOFIELD described the preparation and use of cartilage for the repair of bone defects, chiefly in the skull and facial bone, caused by infection, congenital failure of development, or the excision of tumours. This was implantation rather than true grafting, since preserved human or animal cartilage was used. Mr. Schofield described how he prepared human costal cartilage from donors aged 17 to 35, and ensured bacterial sterility during storage at 0° C. in 1 : 4,000 "merthiolate." He was now also trying whale scapula (a whale has no costal cartilages). The immediate problems were mechanical—the avoidance of warping of the graft and getting a snug fit. There was no difficulty with an immunity response, probably because cartilage was largely mucopolysaccharide and contained little protein. But there was a slow foreign-body reaction, with absorption of the implant and its replacement by fibrous tissue over the course of a year or so, and they were seeking ways of delaying this.

In the discussion Dr. L. M. FRANKS showed small pieces of mouse tumour grafted into the anterior chamber of the guinea-pig eye. They were invaded by blood vessels and plasma cells from the host, and usually survived one to two weeks, but occasionally longer. Transplanted into the guinea-pig lens, tumour cells survived at least 4½ months: vascularization was slow or absent.

Mr. H. H. G. EASTCOTT described a man who had had a homologous arterial graft and a year later was regrafted with a further 20-cm. length of artery. The old graft and some adjoining artery were excised and examined. The graft, unlike the host artery, showed no arteriosclerosis and was not thrombosed. None of the original cell pattern could be defined, but elastic tissue had persisted well, so that the graft had remained functional.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Keratoplasty with Acrylic Implant

SIR,—Keratoplasty has made slow but steady progress during the past two to three decades, especially on the Continent, where there is an abundant supply of human donor material. Recent legislation should in the near future ensure an adequate supply of human corneal tissue for the use of ophthalmic surgeons throughout this country. A very high percentage of successful corneal grafts become opaque in a year or two, probably owing to some allergic tissue reaction. One of us (J. M. A.) suggested that this unfortunate tendency might be overcome by substituting an acrylic inlay. Various techniques were tried by the writers and Mr. B. Thorne Thorne on rabbits and enucleated human eyes, but it was surmised that the living corneal epithelium would recede after a time and grow underneath the implant, and then reject it. The following case shows that this catastrophe need not occur.

A woman, aged 48, with corneal opacities due to interstitial keratitis, and both lenses opaque, expressed her willingness to have the operation. The patient and her family were aware that the chances of success were remote. Her visual acuity was reduced to bare perception of light, and she had been registered as blind within the meaning of the Act for many years.

Using a Franceschetti type of trephine, a central corneal disk 5 mm. in diameter and 0.3 mm. thick was removed from the right eye on June 15, 1952 (D. G. M.), and the cornea undermined approximately 2 mm. all round. Three radial snips were then made at 12, 4, and 8 o'clock, and corneal sutures inserted but left untied. These were used to lift the corneal flaps to facilitate the insertion of the transparent acrylic implant, which was 0.3 mm. thick, 6.5 mm. in diameter, and had an anterior radius of curvature of 7.8 mm. The corneal sutures were then tied, and, for additional security, two double-armed perilimbal sutures were used with their centres at 6 and 12 o'clock and 3 and 9 o'clock respectively. It was realized later that these transverse sutures were unsatisfactory and caused some degree of tilting. On July 1, 1952, the edge of the inferior quadrant of the implant from 3 to 6 o'clock presented and lay external to the corneal flap. It was decided to reinsert the implant and rely purely on the corneal sutures. During this procedure it was noted that the underlying corneal tissue was clear and smooth. Shortly after this, however, the whole cornea became vascularized and opaque, and this was not controlled by subconjunctival injections and cortisone drops. The eye slowly, but steadily, quietened and gradually the corneal epithelium spread *over* the implant, not under as was expected, and completely enclosed it. Repeated examination during the last few months shows progressive clearing not only of the new epithelium over the implant but also of the cornea as a whole. The eye is white and the vascularization has practically disappeared. The implant now appears to be quite secure, and the corneal epithelium is so smooth that it may be possible to do a lens extraction in the near future.

This case is reported to stimulate criticism and discussion. Perhaps some with more experience of corneal grafting and better equipment could improve the technique and obtain better results. We believe that a 3-mm. trephine and an implant of 5 mm. diameter would be adequate and cause less reaction. Instead of transverse and vertical fixation sutures, a ventilated contact shell, or possibly a complete conjunctival flap, could be tried for protection. Also, earlier use of cortisone might minimize or prevent vascularization. As a point of interest, the trephine and transparent acrylic implant were made locally.—We are, etc.,

D. G. MACPHERSON.
J. M. ANDERSON.

Hove.

Compressive Lesions of Peripheral Nerves

SIR,—I was most interested in the article written by Drs. Hugh Garland and Doreen Moorhouse (December 27, 1952, p. 1373) and noted their comment: "The student or practitioner is not, however, so familiar with more prolonged states of external popliteal paralysis. . . ." From my own small experience I have collected in one year of National Service in the Royal Navy three cases of what might be called "compressive lesions of peripheral nerves."

External Popliteal Nerve Palsy.—A seaman rating, aged 24, as cox of a clinker four sat with legs crossed and knees resting just outboard so that the gunwale pressed against the head of each fibula as each onward surge of the boat occurred. When he got out he found great difficulty in walking, and had to be helped back to the ship. Here I examined him and found a complete right external popliteal nerve palsy with associated hypoaesthesia of the lateral aspect of the leg; he had no pain. Recovery was complete in two weeks.

Median Nerve Palsy.—A steward, aged 22, slept for an hour with his right arm tucked under his body. On awakening he noticed loss of sensation in his fingers; on examination an area of anaesthesia was found which included the thumb, index finger, and middle and radial half of the ring finger and extended into the palm; there was loss of power of the small muscles of the thumb and inability to flex the index finger adequately. No pain was complained of and recovery of motor function occurred in five days; recovery of sensation took four weeks.

Radial Nerve Palsy.—A leading-seaman, aged 31, had been for a picnic with his wife; during the afternoon he put his arm around her and they both fell asleep. He was awakened by severe pins and needles in his right arm and found himself unable to move his wrist. The following morning he had a complete radial nerve palsy with wrist drop; the triceps was not involved, and he had no pain. Recovery took six months.

I saw all these cases within 24 hours of the initial compression, and all were complete with the possible exception of the median nerve palsy. Drs. Garland and Moorhouse put forward the theory that compression paralysis is initially complete; the above cases seem to agree with their exception. No central neurological lesion was found on examination of these ratings.—I am, etc.,

A. K. FRAZER.

Dissecting Aortic Aneurysm

SIR,—The account by Dr. R. K. MacCuish (January 10, p. 71) of cases of dissecting aneurysm of the aorta draws attention to the difficulties of correct diagnosis during life. I was interested to note that in Case 5 the man had had a transient numbness and weakness of his left leg.

I was saved from operating on a similar case by my house-surgeon, who drew attention to the fact that in his history the man had described a transient loss in the use of his legs, and my house-surgeon had seen a previous case proved at necropsy. I believe this is a recognized occurrence and I have subsequently seen two similar cases where transient loss of use of one or both legs had been proved at necropsy to be associated with a dissecting aneurysm of the abdominal aorta. I cannot recollect who first drew attention to this phenomenon, but I believe that the explanation may be that the patient has a temporary ischaemia of the spinal cord resulting from spasm of the lumbar arteries at the time of the dissection.—I am, etc.,

C. PATRICK SAMES.

Bath.

Analysis of Articular Cartilage

SIR,—Resilience is the pre-eminent characteristic of healthy articular cartilage. As Dr. C. H. G. Price (January 24, p. 218) points out in discussing my article (December 13, 1952, p. 1295), the importance of the degree of hydration, as well as the relative amounts of collagen and chondroitin sulphate, in determining the physical features of articular cartilage must not be overlooked.

This was taken into account in my work, but, in order to exclude variation due to hydration, estimation of collagen and chondroitin sulphate was exclusively performed on material dried to constant weight and results expressed as collagen/chondroitin sulphate ratio.

Dr. Price may, however, be interested to know the figures for total water content in some samples analysed:

Articular Cartilage. Knee: Femoral Condyles	Water Content %
Weight-bearing: Lateral	73·0
Medial	73·8
Non-weight-bearing: Lateral	73·6
Medial	73·8

In a comparison of the mean water content of weight-bearing and non-weight-bearing articular cartilage from four cases the difference is negligible ($t=0.33$, $P=0.7$–0.8).—I am, etc.,

Taplow, Berkshire. BRYAN F. MATTHEWS.

Electrolyte Changes and Paralytic Ileus

SIR,—We should be grateful if you would permit us to reply to comments made by Mr. T. J. Noonan (October 4, 1952, p. 777) and Dr. J. Drummond (December 6, 1952, p. 1257) on our paper on paralytic ileus published in the *Journal* of September 13, 1952 (p. 587).

Mr. Noonan considered that we had too lightly dismissed the use of intestinal intubation in paralytic ileus. Since our paper was primarily concerned with electrolyte and endocrine aspects of paralytic ileus, and was not intended to be a comprehensive review of the subject, no more than passing reference could be made to the usefulness of long intestinal tubes. The virtues of decompression by intubation have been adequately extolled in other publications[1] [2] though seldom, if ever, with any appreciation of the possibility that concomitant attempts to correct fluid and electrolyte deficiencies might make at least as great a contribution to the patients' recovery as the decompression *per se*. We mentioned that intestinal drainage by suction serves a useful purpose, at least symptomatically and in reducing complications, and we recognize that bowel distension, and, indeed, other factors, may contribute to the impairment of motility in full-blown paralytic ileus in man. The return of normal bowel evacuation in spite of the persistence of distension in several of our patients, however, and the observation that the intestine is able, after electrolyte deficiencies have been corrected, spontaneously to overcome distension without effective decompression through an intestinal tube, provide strong evidence against the primary aetiological importance of distension. At present the evidence which supports the view that distension contributes to the paralysis of the bowel is restricted to, first, animal experiments in which the intestine has been damaged or paralysed by pressures greatly in excess of any which have been recorded in human paralytic ileus; and, secondly, human patients with ileus in whom recovery has followed the use of intestinal suction, usually together with attempts to correct fluid and electrolyte deficiencies and other measures. This evidence does not seem to be conclusive, but it is wise, nevertheless, to continue the use of gastro-intestinal suction. We would perhaps share Mr. Noonan's enthusiasm for the Wild and Grafton–Smith long intestinal tubes if they prove easier to pass in the critically ill patient than were the Miller–Abbott, Cantor, and Harris tubes.

Dr. Drummond has criticized our suggestion that the high urinary losses of potassium and the electrocardiographic evidence of potassium deficiency found in patients with paralytic ileus might have been attributable to the abnormal persistence of adrenocortical hyperactivity, as reflected in the prolonged eosinopenia. Instead, he considers that, while adrenocortical secretion might well have continued in these patients, it was insufficient to meet the needs of the individual. To substantiate his point, Dr. Drummond mentions that he has used hormones with great success in the treatment of ileus, and we look forward with interest to hearing further details of these findings. Since Dr. Drummond was careful to correct the electrolyte abnormalities in his cases, however, it might be difficult to be sure that his patients' improvement was the result of hormone administration, and not simply the effect of overcoming potassium deficiency. In our cases adrenocortical activity was not only present, as shown by the persistent eosinopenia, but was actually producing intense metabolic effects such as almost complete retention of administered sodium and chloride when the plasma concentrations of these ions had been restored to normal. These changes were usually reversed at the time of recovery, and we cannot, therefore, agree that there was any indication of inadequate adrenal activity. All the present evidence pointing, as it does, to hyperactivity of the adrenal cortex, we would hesitate to use A.C.T.H. or cortisone, which might be expected to aggravate rather than improve the condition.—We are, etc.,

D. H. P. STREETEN.
J. N. WARD-MCQUAID.

Oxford.

REFERENCES

[1] Peters, J. P., *et al.* (1941). *Problems of Intestinal Obstruction*. Univ. of Pennsylvania Press, Philadelphia
[2] Devine, J. (1946). *Brit. J. Surg.*, 34, 158.

Damages Against Casualty Officer

SIR,—I was horrified to read in the *Journal* of January 17 (p. 166) that £2,640 damages had been awarded against a casualty officer for failing to admit to hospital, or asking a consultant to see, a patient whose only presenting symptoms were bruising of the abdomen and slight shock.

If casualty officers admitted to hospital, or called in a consultant, every time a patient with similar injuries presented himself the present National Health Service in hospitals would become unworkable without a big increase in staff and beds.

I would welcome a return to the days when a little more respect was shown to medical men and the public was a little less ready to make capital out of their occasional failings. Patients are becoming very mercenary; how many of us, working in hospitals, have noticed the remarkable cures in patients when at last their compensation claims have been satisfactorily settled.—I am, etc.,

Boscombe, Hants. M. V. GUILMANT.

SIR,—As resident hospital officers with responsibilities in the casualty department, we are most distressed to read of the case of damages against a casualty officer (January 17, p. 166). It appears to us that the officer is a victim of two separate and gross injustices. First, we do not believe that, on the evidence reported, there is any suggestion whatsoever of negligence on his part. Secondly, does the Court consider that management committees have ceased to be responsible for the actions of their employees?

Apart from the injustice involved to an individual, it seems to us that the decision of the Court has set a precedent which will make any sensible practitioner think more than twice about undertaking casualty responsibilities in future.—We are, etc.,

RICHARD MACKIE.
STANLEY C. SIMMONS.
HENRY H. HAYES.
DENIS KELLEHER.

Harold Wood, Essex.

SIR,—There must be many doctors who will have read the account of the legal proceedings entitled *Payne* v. *St. Helier Group Hospital Management Committee and Another* in the *Journal* (January 17, p. 166) with dismay and apprehension and would like the unfortunate victim to know that in their opinion justice has hardly been done. According to the account a casualty officer made a full clinical examination, including auscultation, of a case of blunt injury to the abdomen and decided it was safe for the patient to return home and remain under the supervision of his own practi-

tioner. The patient ultimately died following perforation of the caecum, and considerable damages were awarded against the casualty officer on the ground that he had exercised less than reasonable care.

I write because I too have been guilty of such malpractice. During my first house appointment I saw a railway porter who had been struck in the lower right abdomen with the handle of his barrow a few hours before. He had continued his work. Being young and enthusiastic, I called a friend and together we tested the urine, examined the rectum, and auscultated all quadrants of the abdomen, finding no abnormality beyond bruising of the abdominal wall. I sent the patient home with instructions to call his own doctor if he had any further trouble. When I was summoned before the hospital house governor four days later and was told that the patient had died of peritonitis, I was fortunate in having to face no worse ordeal than a coroner's inquest. There I was entirely exonerated by the university pathologist, who assured the court that there had been primary bruising of the bowel which could not have been detected clinically, and the secondary perforation must have occurred later. The experience was quite enough to teach me a healthy respect for all such accidents in the future.

The verdict given in this case is very disturbing. It shows that a doctor may be heavily penalized for an error of judgment (and which of us is exempt from these ?) when he has been neither careless nor lazy and has taken what many people would regard as adequate precautions against an oversight. It means that the evidence of the only doctor to see the patient is to be disregarded (in this case concerning the absence of rigidity) in favour of a finding that someone else considered afterwards ought to have been there. It means too a serious blow to the liaison between hospital residents and general practitioners, with the consequent need for admission to hospital of innumerable cases of trivial injury. I look forward to an early and successful appeal.—I am, etc.,

Birmingham. W. G. MILLS.

SIR,—The following letter has been sent by us to the secretaries of the Medical Defence Union and the Medical Protection Society:

"We, the undersigned, are greatly disturbed by the verdict in the case of *Payne* v. *St. Helier Group Hospital Management Committee and Another* reported in the *British Medical Journal* of January 17 (p. 166), and hope that you will do all in your power to see that the case is carried to appeal."—We are, etc.,

C. ABRAHAM.
N. BUDGE.
D. W. BULL.
C. P. ELLIOTT-BINNS.
R. R. EVANS.
H. M. FEHILY.
G. S. FOWLER.
B. M. GRIFFITH-JONES.
R. E. HOGG.
D. B. LANGRANA.
T. W. LAMONT.
T. T. E. MICHAEL.
A. C. MORRISON.
R. G. NICHOLS.
A. B. PARTRIDGE.
T. TENDERENDA.
G. W. WADDY.
C. J. ZERNY.
E. A. J. ALMENT.

Iron Therapy

SIR,—May I be permitted to reply to the letters by Dr. D. Wise (December 27, 1952, p. 1415) and Dr. R. S. Saxton (January 10, p. 97) in this single letter? It is valuable to note that the same results can be obtained by two differing arithmetical procedures. It certainly emphasizes the importance of my *clinical* observations. I am interested in the calculation of the coefficient of iron utilization which Dr. Wise sets out, and accept his statement that it is inversely proportional to the intensity of ferro-therapy. Of course Witts worked out his coefficient of utilization by a different route, and undoubtedly his cases were correlated with the clinical result. I should like to point out that my use of the same coefficient was also correlated with the clinical result, and I should like to stress that my cases, using organic iron, were amazingly more fit than the control cases. I must apologize for certain minor arithmetical errors. These errors crept in purely as typing mistakes, and are obviously of little significance.

To deal with Dr. Saxton's question, whether ferrous gluconate by itself is a more efficient haematinic than ferrous sulphate or iron ammonium citrate given without those vitamins, the answer is yes. The papers by Jasinski and his co-workers, which I quoted, clearly indicated this fact. It has long been known that vitamin C is an important factor in the prevention of anaemia. Captain Cook used to treat scurvy and anaemias occurring during his voyages by the exhibition of vitamin C, and his cases improved out of recognition. There is abundant evidence that vitamin-B absorption can be upset in simple anaemias, therefore it is justifiable, on therapeutic grounds alone, to include both the B and C complex in a mixture containing an acceptable organic iron salt. I fail to see the need for further investigations on patients when the work has already been carried out many times and the results are so well known. Finally, I must point out that the beneficial effects of the exhibition of the mixture are so great that they outweigh any theoretical objection.—I am, etc.,

London, W.1. DAVID HALER.

Treatment of Pernicious Anaemia

SIR,—In my letter (November 29, 1952, p. 1204) I gave details of a case of megaloblastic anaemia which was treated initially with a well-known parenteral extract of liver with an excellent haematological response before he was permanently improved with proteolysed liver. This case could not have been an example of "idiopathic refractory megaloblastic anaemia" only responsive to crude liver extracts by mouth or sometimes to folic acid, as suggested by Dr. E. K. Blackburn *et al.* (December 20, 1952, p. 1360).

I have nine cases of pernicious anaemia attending my clinic, six which are maintaining better blood counts with injections of liver, and three with proteolysed liver by mouth, than when they were treated with adequate amounts of vitamin B_{12}. After studying the results of the treatment of over 100 cases of pernicious anaemia during the past five years I am convinced that it is an over-simplification to hold the opinion that it is preferable to use vitamin B_{12} in the treatment of all the usual cases of pernicious anaemia. I repeat that injections of crude liver, vitamin B_{12}, and proteolysed liver by mouth are all useful in the treatment of ordinary cases of pernicious anaemia.—I am, etc.,

Birmingham, 18. R. O. GILLHESPY.

Thiouracil in Toxic Goitre

SIR,—I would like to thank Mr. Denis Hindmarsh for his letter (January 17, p. 158) commenting on the article by Dr. Agnes T. Kennie and myself on thiouracil in toxic goitre (December 27, 1952, p. 1387). We seem to be in general agreement.

With regard to the mortality from surgical treatment of the condition, we realize that much better results than the suggested figure of "not more than 2%" are achieved in special centres, and we did make this point in the article. Mr. Hindmarsh's experience of 200 cases must place him in that category. We feel, however, that, just as thiouracil is used all over the country, so also is thyroidectomy, and the general results are not accurately known.—I am, etc.,

Glasgow. DAVID DOUGLAS.

Butazolidin

SIR,—May I, too, be permitted to comment on your leading article (December 27, 1952, p. 1401) and annotation (January 31, p. 267) on "butazolidin"?

The effects of the drug on joint swellings and E.S.R. have already been satisfactorily noted, particularly in acute cases. I have had ample opportunity of using the drug, and have in recent weeks studied the case reports on some of the deaths. The toxic effects have been reported with a degree of hysteria in the popular press, and the efficacy of the drug,

if used wisely, not sufficiently stressed or entirely overlooked. The majority of the cases that developed trouble came into several categories. First, the senile patients with very little cardiac reserve were thrown into decompensation or developed pulmonary oedema. Patients with hypertension of long standing were given doses of 1,200 mg. per day. Such high dosage is seldom, if ever, justified in the younger age groups. In several of the deaths reported other drugs were given at the same time. These drugs could in themselves produce gastric irritation or agranulocytosis. The ability of butazolidin to produce haemorrhage from the stomach is very puzzling, as butazolidin is insoluble in an acid medium, and it is difficult to conceive that an undissolved drug can cause much direct irritation. It may well be due to some systemic action which takes place after absorption.

It is entirely wrong in my opinion to give a few weeks' supply of the drug to a patient whose tolerance is not known. In one case reported a patient was given a further three weeks' supply after reporting that she was already suffering from a sore throat. It is unjustifiable to assume that butazolidin caused agranulocytosis in this particular case in view of the fact that the first blood count was not taken until after at least four other drugs had been employed. Mismanagement is often responsible for the deaths or toxic manifestations.

There has been too much tendency on the part of investigators to regard butazolidin as a simple analgesic. This, in the mind of the general practitioner, may engender careless prescribing habits. Butazolidin is not a simple analgesic but a potent anti-rheumatic agent with serious toxic potentialities, and should be treated with the same respect as cortisone or gold. When properly used the therapeutic benefits to be derived are so great as to outweigh by far the toxic hazard. Emphasis must be laid, therefore, on low dosage, frequent blood counts, careful clinical observation of the patient, and careful selection of cases, avoiding the senile, the chronic arthritic with irreversible bony changes, or the hypertensive with poor cardiac reserve. Used in this way, and avoiding the riotous enthusiasm of the inexperienced, much relief can be given to a multitude of suffering patients. —I am, etc.,

Manchester. HUGH SELBOURNE.

Succinylcholine

SIR,—Reviewing the drug succinylcholine in your annotation (January 17, p. 148), and in particular the work of Evans *et al.* (p. 136), there was criticism of the fact that these workers had failed to show the apnoeic effect of successive doses of the drug.

From the use of succinylcholine in patients undergoing courses of E.C.T., it had been noted how regular was the duration of apnoea following a fixed dose in a given individual. Impressed by this fact, careful note of the length of apnoea was made in those cases requiring repeat doses of the drug during a single anaesthetic. It was found that equal doses produced similar periods of apnoea. This seems to be in keeping with the findings of Kay (*Lancet*, 1952, 2, 200).

Perhaps, Sir, this information will help to remove any doubt that your article has caused.—I am, etc.,

Wallington. B. L. DAY.

College of General Practitioners

SIR,—We write to add our protest to that so admirably expressed by Dr. Bernard Kendrick (January 10, p. 97) against the method adopted by the Steering Committee in presenting us with yet another *fait accompli*.

It was stated in the *Journal* (January 24, p. 229) that 1,000 doctors have now joined the College of General Practitioners. As this represents about 5% of general practitioners, it would appear to indicate that there has not been the overwhelming support anticipated, due, no doubt, to the undemocratic method of formation and presentation. According to Dr. H. H. Pilling, in an illogical letter (January 24, p. 219), this college is only for the few enthusiasts and there is to be no effort made to make it a college of *all* G.P.s, in which case it is doomed to failure from the start. It could only dispense distinctions within its own ranks, and interfere with the work of the existing negotiating body and other established authorities.

Mr. A. Wilfrid Adams (p. 218) considers that the College is necessary to raise our prestige. We do not doubt Mr. Adams's sincerity in the least, but surely in this case his altruistic principles have carried him away from practical realities. With whom is it necessary to raise our prestige? If with the specialists, how will we be able to impress them with our merit more than we can now? In this area, at any rate, the majority of the more senior specialists know what we are worth and treat us accordingly. We trust that some of the younger members of hospital staffs will mellow with time. If with our fellow practitioners, surely by now we know one another for what we are worth. If with the patients, and we undoubtedly have lost standing with them, it is another matter. As we see it, the main cause of the lowering of prestige is that doctors have to work to rules, but patients are free to please themselves and impose on the doctors as much as they like without fear of retribution. As long as this holds there can be no improvement. As the negotiating body, the B.M.A. is the only organization that is competent to deal with it. Surely at this stage efforts should be made to ascertain the real attitude of all G.P.s to a College of General Practitioners, and to rouse them from their lethargy before proposals which they do not support become established practices.—We are, etc.,

J. P. DENNY. D. L. ISAAC.
C. H. HIGHFIELD. A. MURPHY.

Long Eaton, Notts.

SIR,—To determine what should entitle a general practitioner to a diploma (if such is to be instituted) of the College of General Practitioners will be no easy task. Clearly it must not be a mere matter of paying a fee and undertaking to do a three days' annual refresher course. If such a diploma is to be something worth having it must be hard to come by; and, if hard to come by, all but the most idealistic will need an incentive, probably financial, to secure it. Like Dr. Ronald A. B. Rorie (January 24, p. 219), I see no alternative to an examination of some kind.

Moreover, it is not true to say that "once a good general practitioner always a good general practitioner." Unlike port, many of us tend to deteriorate with age. I suggest, therefore, that a diploma should be tenable only for a limited period, say, five or seven years, at the end of which —and each subsequent similar period—it should require renewal either by further examination or on other sufficient evidence that the candidate is not obsolescent—or even obsolete.—I am, etc.,

Crediton. L. N. JACKSON.

Overfeeding in Early Infancy

SIR,—In view of the frequency with which overfeeding is diagnosed in infancy to-day it is surprising that so little adverse comment on my paper (November 29, 1952, p. 1178) has appeared in your columns.

My reason for writing now is to underline Sister E. Morrison's comment (January 17, p. 160) that it is easy to underfeed the bottle baby. In his letter (January 10, p. 99) Professor C. Wilfred Vining has drawn attention to the reason for this—namely, the inadequate feeding quantities on the packets of dried milk. It may not be generally appreciated that the instructions on the tins of full cream national dried milk allow rather less than 50 calories per lb. for babies of all ages and sizes. I have drawn attention elsewhere (*Arch. Dis. Childh.*, 1952, 27, 449) to the stoking-up period in the first two months of life when some babies have the potentiality to gain as much as 16 oz. (0.45 kg.) per week. This rapid rise is quite uncatered for at present,

but a sliding scale of diminishing numbers of calories per lb. would meet the case. Until this is provided, the claim on the tins that the quantities have been "scientifically worked out" is unjustified.

More important, however, is the large number of parents of young babies who, through fear and ignorance, are forced to pace the floor day and night with their hungry offspring. A new baby should be a welcome addition to the family, but too often he is a fretful, howling menace. It is within our power to put this right in the case of the bottle baby at least.—I am, etc.,

Stock, Essex. IAN G. WICKES.

The Backward Child

SIR,—The mind of the child does not conform to any set pattern. It is capable of an almost infinite series of modifications. Dr. D. J. Salfield in his criticism (January 10, p. 96) of my article underestimates the extent of the departure from the mean which can occur in children. His confidence that no child psychologist or psychiatrist would be deceived by "shyness" or "inhibited co-operation" is, in my experience, quite unjustified. My colleagues here, and myself, have had on a number of occasions the pleasant experience of finding that our original, always very tentative, estimate of a child's ability proved to be unduly low. Still more often have we found that in the case of very young children the necessarily brief examination by outside medical authorities has produced a misleadingly low estimate.

Almost all the responses measured in test situations are affected by the child's previous experience. To this extent they are "educational." The institutionalized child has not had the necessary education to cope with some tests, though he may have the necessary ability. This applies, for example, to the picture vocabulary of the Terman–Merrill version of the Binet–Simon. We find here that children who have long been in institutions have never seen a penknife, stool, rifle, basket, or house of the type represented, nor have they been coached by their parents—as they are mostly "deprived" children—in the use of appropriate verbal responses for these pictures. Dr. Salfield apparently also assumes that testing prior to certification as ineducable or mentally defective is generally done by child psychiatrists or psychologists. In general this work is done by school medical officers who may have a great many other duties and may have little time or opportunity to develop skill in this aspect of their work.

It is for these reasons and others that my colleagues and I at the Fountain Hospital have put forward the view that legal certification of ineducability and of mental deficiency should be deferred until the age of 5. If this principle were included in new legislation it need not preclude admission to hospital for any necessary treatment or observation at any earlier age by arrangement with the parents.—I am, etc.,

London, S.W.17. BRIAN H. KIRMAN.

Impetigo Contagiosa

SIR,—Professor Robert Cruickshank mentions in his Malcolm Morris lecture (January 10, p. 55) that the subject of impetigo contagiosa is a controversial one, and we feel sure that he would be disappointed if everyone agreed with his views. We certainly do not agree with his statement that streptococcal impetigo is the common contagious infection of schoolchildren and that staphylococcal impetigo is mainly a disease of adults and that there is little evidence that it is contagious. Stuart-Harris,[1] reviewing the arguments on the aetiology of impetigo, includes the work of Bigger and Hodgson,[2] Sheehan and Fergusson,[3] and Twiston Davies *et al.*,[4] which are quoted by Professor Cruickshank, and comes to the conclusion that the haemolytic streptococcus is essentially a secondary invader. Our findings strongly support this view. In our experience the clinical entity of streptococcal impetigo is rare and the common disease amongst children is the circinate bullous impetigo which Professor Cruickshank quite rightly described as staphylococcal impetigo. It is highly contagious and family spread is common.

During the last two years 105 bacteriological investigations have been carried out on cases of impetigo referred to our department. A considerable number of these had not received treatment with antibiotics. Staphylococci were found alone in 93 and in combination with haemolytic streptococci in 12. No clinical distinction could be made out between the pure staphylococcal cases and those with a streptococcus present. Nor do we agree that impetigo is a disappearing disease, since its reappearance in this area, particularly amongst children, has already been reported (Sneddon[5]). On theoretical grounds the fact that impetigo is once more increasing suggests that it must be largely staphylococcal in origin, since haemolytic streptococci do not become penicillin-resistant and they should have all been swept away in the avalanche of penicillin ointment which has fallen on the inhabitants of these islands in the last few years.—We are, etc.,

R. E. CHURCH.
I. B. SNEDDON.
H. R. VICKERS.

Sheffield.

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Rheumatic Carditis

SIR,—In your leading article (January 3, p. 34) commenting on Professor Geoffrey Hadfield's Carey Coombs memorial lecture you ask: "Why is there no correlation between the severity of the initial angina and the intensity of the carditis?" The answer to this question, which my own experience indicates as being the correct answer, is that there *is* a very definite correlation.

The manifestations of rheumatic infection which succeed (after the usual interval has elapsed) an attack of acute tonsillitis are almost always more acute, and the carditis and subsequent cardiac damage much more severe, than when the rheumatic attack was not preceded by an acute angina. Of the rheumatic children, many thousands in number, who have been treated in the rheumatism unit of Queen Mary's Hospital for Children, Carshalton, Surrey, it was almost invariably found that the worse the initial sore throat the worse the cardiac involvement.

In 1937 I made an analysis of certain facts relating to children admitted to the rheumatism units then controlled by the London County Council. Of 1,000 non-selected admissions it was found that in only 53 of them had the attack been preceded by a really acute tonsillitis, and in 70% of those 53 children gross and permanent cardiac damage developed. This percentage is about double that which was found when all types of attack were included in the analysis.—I am, etc.,

Carshalton, Surrey. C. E. THORNTON.

"Unfit for Military Service"

SIR,—I am concerned at the apparent increase in certificates lightly given by medical practitioners, both general and specialist, stating that a patient is unfit to do his National Service. It is not the numerical increase that worries me so much as the unthinking and often unfortunate way in which these certificates are given, so that considerable harm is done on all sides. I am able to see both sides of this because I hold a civilian appointment and, quite separately, an advisory one to one of the Services.

The harm is first done to the patient, who forms the view that either he or Service life is unhealthy; this is usually quite absurd, and in fact Service life is often the saving of a nervous and coddled young man. Secondly, harm is done to the parents, who have probably visited the doctor and often paid a fee with the purpose of acquiring such a certifi-

cate, and who then develop a paranoid outlook to life in general and the Service in particular when their son is asked to serve after all. Thirdly, harm is done to the Service, because this situation often leads to a ministerial inquiry and a "question asked in the House" and the whole issue may become political, with the added suggestion that Service doctors are poor clinicians. In fact it is probably true to say that never has clinical ability in Service doctors been higher than it is now. It is, of course, most valuable to have a balanced and experienced opinion on a National Serviceman from his own doctor or a competent specialist. I have noticed that those doctors who have known something of Service life themselves never give the type of certificate about which I am concerned.

My particular interest brings me into contact with certificates about "blackouts" and headaches. Nothing is more helpful than a good description by an unbiased observer of an attack of unconsciousness, and nothing more harmful than the last certificate I read, which stated: "I have examined X. Y. Z., who is suffering from neurocirculatory asthenia and is quite unfit for any form of military service." The signature was grandiose in its self-description; and, in fact, the boy was suffering from mild attacks of migraine which had not interfered with his earning capacity (£14 a week) before joining the Army. My plea is for more care and thought in the giving of these certificates, particularly in cases of vasomotor syncope, which is often due to muscular flabbiness and for which the physical training of Service life is one of the best forms of treatment.—I am, etc.,

Ashford, Middlesex. A. BARHAM CARTER.

Sarah Gamp's Pharmacopoeia

SIR,—It may be that Mr. J. A. Ross, in his inquiry regarding "slime draught" (January 10, p. 102), has failed to appreciate the language difficulties of the late Nurse Gamp. Like many of Dickens's characters, Mrs. Gamp had a gift for mispronunciation, and therefore might quite easily use the word "slime" where "saline" was intended. Saline draughts, consisting of sodium bicarbonate mixed with a vegetable acid, were common in her day, being employed, according to Pereira, as diuretics and lithontriptics. In *Elements of Materia Medica* (1839) Pereira warns against their use in the treatment of phosphatic deposits in the urine, and quotes Dr. Prout's words, "Were I required to name the remedy calculated to do the most mischief, I should name the common saline draught, formed of potash or soda, and some *vegetable acid*." Possibly Dickens had heard of this and wished, by revealing the type of noxious physic with which Sarah sped her charges on their way, to blacken further the character of a great lady.—I am, etc.,

London, S.E.12. W. A. LITTLEJOHNS.

Has the Report a Pathology?

SIR,—My colleague, Professor Lambert Rogers, complains (January 24, p. 215) of the misuse of the noun "pathology." May I add my complaint of the more frequently misused adjective "pathological" in such phrases as "pathological department" and "pathological report." I think the point is made clear by the following anecdote. On asking the whereabouts of some missing students, I was told that they were in London having a "gynaecological examination."—I am, etc.,

Penarth, Glam. A. G. WATKINS.

Attempted Suicide by Burning

SIR,—The case of attempted suicide by burning reported by Mr. R. J. V. Battle and Dr. H. E. S. Marshall (December 27, 1952, p. 1397) prompts me to recall a somewhat similar case.

A married woman of 59 was admitted to a mental hospital as a voluntary patient seven weeks before being transferred to a plastic surgery unit. Her admission to the mental hospital followed a suicidal attempt in which she bundled some newspaper between her legs and then set fire to it. She had previously been complaining of depression and tiredness, inability to concentrate, and ideas of unworthiness. She was retarded and at first unwilling to have treatment because she felt so wicked and did not want to get better. Following a course of E.C.T. (seven treatments in all) her depression disappeared completely and she became pleasant and co-operative. On admission to the unit she was found to have moderately extensive burns of full thickness skin loss affecting the antero-medial aspects of both thighs and suprapubic region extending on both sides to the vulva. The areas were covered by healthy granulations, and skin grafting was successfully undertaken. She was discharged home after four weeks, and when reviewed finally some eight months later the grafts were satisfactory and she had remained in good health and mentally quite normal.—I am, etc.,

Basingstoke. D. A. CAMPBELL REID.

Malignancy in Undescended Testis

SIR,—The development of malignancy in an undescended testis is described in most textbooks, and is given as an argument in favour of removing the testis when it is not possible to place it in the scrotum. Imperfect migration of the testis is very common, but malignant changes are very uncommon, so perhaps this case may be of interest.

A clerk of 37 years came to see me on September 29, 1952, complaining of a swollen abdomen. He had complained of "gastritis," fullness after meals, flatulence, and indigestion for nine months, and later of loss of energy, loss of weight, slight constipation, and recently of vomiting. Pain was absent. On examination he was 5 ft. 1 in. (1.55 m.) tall, and weighed 7 st. 5½ lb. (46.57 kg.). He had a congenital ptosis of the left upper eyelid and a sebaceous cyst on each side of his face. His abdomen was completely filled by a large hard mass. No testis was present in the left side of the scrotum. He had a marked degree of hypospadias, the urethra opening well down in the scrotum. When I advised surgical treatment he solemnly asked if I thought it was really necessary.

On October 2 I opened his abdomen through an incision from xiphisternum to pubes, and found a solid tumour lying free in the peritoneal cavity and attached by a large pedicle in the left inguinal region. It was easily removed. The only signs of secondary deposits were three or four small nodules on the pedicle, and one on a small omental adhesion; these were removed at the same time. He went home in a fortnight, and came up to see me on November 16, 1952, weighing 7 st. 11 lb. (49 kg.), feeling well, and with no signs of trouble.

The tumour removed weighed 10 lb. 14 oz. (4.9 kg.) and measured 12 by 9 by 4 in. (30.5 by 22.9 by 10.2 cm.). It was 33 in. (83.8 cm.) in circumference. The pathological report (Dr. E. Travers) described the tumour as smooth and round in outline, composed mainly of necrotic tissue, the sections showing a seminoma of the testis.

The interesting points in the case are the large size of the growth, the ease of removal, and the associated congenital abnormalities.—I am, etc.,

Rotherham. ERIC COLDREY.

Advertising in Examinations?

SIR,—The old controversy about the correct names for drugs mentioned in examinations has again arisen. I remember something of the sort in the Cambridge M.B. Oddly enough the drug then was one used most by anaesthetists—"coramine." It was considered at the time most underhand to call it nikethamide, a name decided on barely two months before. I have not seen the paper referred to by Drs. H. C. Churchill-Davidson and W. D. Wylie (December 20, 1952, p. 1361), but I wonder if "flaxedil" was one of the drugs in question? I consider its official name (gallamine triethiodide) a mouthful, and difficult for nationalities in which "th" is unpronounceable. I know that examinations in theory are held to determine the knowledge of the entrant, but often in practice they seem to search out what he does not know. In fact, one examiner in this particular examination asked in the viva why "avertin" is, or was, so named. I took the trouble to have its original German manufacturer telephoned, and was assured that there was not, nor had been, any special significance in the name.

In Holland, at any rate, there is considerable interest in the British educational system, with special reference to post-graduate diplomas. I am always encouraging assistants to try to be accepted to sit for these examinations. I feel strongly that any element of precise insularity should be discouraged. The name chosen by the makers of a new drug is the one which usually gains common usage. The wise candidate should surely state in his answer what the precise nature of the compound is, thereby gaining an extra mark, and I doubt if the advertising of it in a paper will make him go home and "use no other."—I am, etc.,

Amsterdam. J. M. B. POOLEY.

SIR,—Dr. L. M. Franklin (January 10, p. 98) writes about the frequent use of the trade names of drugs by hospital doctors. I can remember as a medical student being frequently disturbed by this tendency in our hospital teachers. Perhaps I was more conscious of it than most of my fellow students because my father was a pharmacist with a healthy contempt for doctors who habitually prescribed proprietary medicines. I can well remember his outburst of indignation when I told him that one of our clinical teachers had advised us always to prescribe a well-known proprietary brand of aspirin in order to be sure of getting a good-quality drug. I can also remember my faith in the exalted being rudely shaken when, in my final year, having bought a textbook of medicine written by an eminent London physician, I discovered a reference to "glycothymoline" in the first chapter.

Perhaps it is unfair to single out hospital practitioners as the main offenders (though surely it is not too much to ask that those with teaching responsibilities should be beyond reproach in this respect). Is not the word "vaseline" frequently on the lips of nearly every medical man? Indeed, so familiar has this proprietary name become that the firm concerned has considered it necessary to insert a notice in their advertisements pointing out that it *is* their registered trade name.—I am, etc.,

Bangor. G. P. WALLACE.

Chronic Staphylococcal Infection in the Baby

SIR,—I was most interested in Professor Alan Moncrieff's Charles West lecture on "Infection in the Newborn Baby" (January 3, p. 1). With regard to his suggestion that there may be a genetic factor in neonatal immunity, I would like to suggest that the failure of babies (and, indeed, of adults) to immunize themselves against the staphylococci causing their sepsis is due to the fact that the site or sites of inoculation and/or the dosage are not conducive to raising their immunity. Ample evidence will be found in Topley and Wilson's *Principles of Bacteriology and Immunity* (third edition, 1946, **2**, chapter 50) that this is a much more likely explanation of the cause of failure than a genetic factor as the main cause.

Further evidence in favour of this explanation is provided by the case of the elder child quoted by Professor Moncrieff, who showed an excellent antibody response to T.A.B. vaccine. Indeed, I would suggest that staphylococcus toxoid, in carefully graduated doses to ensure minimal, or no, local or general reactions, would have done much to cure the case quoted. Personal experience and that of my wife, Dr. P. J. Alexander, has shown that staphylococcus toxoid will cure chronic or recurrent staphylococcal lesions in children as well as in adults, and I am confident that, if used correctly, it would help some babies with such lesions.—I am, etc.,

Hull. J. G. ALEXANDER.

Pulmonary Moniliasis

SIR,—That Professor L. P. Garrod's warning (January 10, p. 95) is well timed is exemplified in a recent case at this hospital. The sputum from a patient with cavitating pneumonia repeatedly grew a profuse culture of *Candida albicans*. This patient responded to antibiotic therapy with complete healing of the five cavities as shown by *x*-ray examination. Antibiotic therapy had been given prior to admission for a febrile illness, and the possibility of Friedländer's pneumonia, as reported by Drs. J. M. Barber and A. P. Grant (October 4, 1952, p. 752), was considered.

I wish to thank Dr. Ronald Lass for permission to mention this case.—I am, etc.,

Maidstone, Kent. HUGH F. CRAWFORD.

Nasal Bleeding

SIR,—In an annotation on "Nasal Bleeding" (May 24, 1952, p. 1124) which has just come to my notice, the treatment of this condition is given in some detail. Cauterization is given as the method of choice, and if this fails we are advised to pack the nose with ribbon gauze and admit the patient to hospital. Few of us who are not rhinologists can be trusted to cauterize the nasal septum without doing harm. Nasal packing is most uncomfortable to the patient, is often ineffective unless done by the expert, and, more important, it may be followed by mastoiditis, although penicillin will diminish this risk.

I am surprised that no mention was made of the treatment of intractable nasal haemorrhage by blowing up a balloon inside the nose. This can be improvised by any doctor or nurse, using a thin rubber finger-stall and a rubber catheter. May I quote from my description of the method in 1932, when it was used in a patient with hereditary telangiectasia ("Hereditary Telangiectasia with Haemorrhagic Tendency," A. F. Hurst and N. S. Plummer, *Guy's Hosp. Rep.*, 1932, **82**, 93)?

"An ordinary soft rubber catheter, about size 7, is passed into an ordinary finger-stall of moderately thin rubber as far as it will go without causing bending or kinking of the catheter, and the neck of the finger-stall is tied tightly with strong fine thread, care being taken not to occlude the lumen of the catheter. This may be dipped in oil or smeared with "vaseline" and is then passed along the floor of the nose as far as the neck of the finger-stall. The patient usually knows which side is bleeding, and if necessary both sides may be plugged. The operator applies his lips to the end of the catheter, holds it in position at the nose, and inflates the apparatus until the thin rubber bag begins to bulge out of the nose. He then clamps the end of the catheter with a pair of artery forceps or other clip and makes certain that there is no bleeding down the nasopharynx; if there is, the pressure is increased.

"The pressure is maintained for 10 to 15 minutes as a rule, though experience in the individual case is the only guide. Then the bag is deflated very slowly, and even when quite empty is left *in situ* for some minutes, either to drop out or to be extracted gently. The procedure can be repeated at any stage if bleeding recommences. The patient soon learns to do it himself and carries the apparatus in his pocket ready for emergency use; it is as well also for him to have a spare finger-stall in case the one bursts. Apart from a slight feeling of distension the patient experiences no discomfort at all.

"No originality is claimed for this very effective method of controlling epistaxis, as it has been used many times before, and it is merely a modification of Cooper Rose's inflating plug,

but it does not appear to be very widely known, and the component parts are always at hand and are very conveniently carried and applied by the patient."

I believe some surgeons teach this method of controlling epistaxis, but why do we not see it used? As a physician I would ask the surgeons if the balloon cannot replace nasal packing in *all* cases of severe epistaxis.—I am, etc.,

London, W.1. N. S. PLUMMER.

Therapeutic Uses of Vitamin E

SIR,—The leading article on "The Therapeutic Uses of Vitamin E" (December 20, 1952, p. 1345) certainly calls for comment by us, the proponents of the use of α-tocopherol in cardiovascular disease.

Such an article might conceivably have been written in 1948 or 1949. However, the picture has changed so rapidly since that time that your leading article now simply does not reflect the findings of investigators in this field. This is best illustrated, perhaps, by the current issue of our medical journal, the *Summary*, which contains the abstracts of 122 reports which have appeared in the medical literature supporting our original contentions. It seems that α-tocopherol shares with Christianity both its beneficence and the observation that those who say it has failed have rarely tried it. Since the American Aristotles first condemned it, too many doctors have dropped a pebble from their own towers to make that condemnation stick.

Briefly, our current *Summary* records that 17 reports have supported us in the use of α-tocopherol for the menopause; 5 in its use for nephritis; 6 for kraurosis vulvae; 4 for capillary permeability; 4 for purpura; 5 for vascular dilatation; 11 for Buerger's disease; 10 for vascular sclerosis; 15 for thrombosis; 3 for muscular power; 20 for indolent ulcers; 14 for diabetes; 4 for Roentgen tissue damage; 4 for incipient gangrene; 2 for wound healing. Finally, 46 reports have supported us in the use of α-tocopherol for heart disease.

It is difficult to believe that all these investigators have duplicated an error. Certainly it is cavalier to dismiss such work in one paragraph. Fortunately, our forthcoming book should help to keep the record straight and we will recommend it to your perusal. Also, as Auden, one of your own poets, has said:

> "One notices, if one will trust one's eyes,
> The shadow cast by language upon truth."

—We are, etc.,

WILFRID E. SHUTE.
EVAN V. SHUTE.

London, Canada.

Control of Bone Growth

SIR,—To the methods of controlling bone length mentioned in your annotation (October 18, 1952, p. 872) I wish to add another—namely, control by radium action on the epiphysial line. This method was employed originally[1] with the object of producing bone curvatures. Thus genu valgum was produced in rabbits[2] by placing radium on the outer side of the knee and genu varum by placing it on the inner side. Right-convex scoliosis was produced in goats and rabbits by placing radium on the left side of one or more vertebrae.

Though the purpose of these experiments was to obtain a circumscribed damage of the epiphysial line, a very marked shortening of the whole radiated bones developed in addition to the anticipated deformities. In one rabbit which had a needle containing 5 mg. of radium inserted for three days on the lateral side of the knee, the femur showed a shortening by 18 mm. after six and a half months, and the tibia of the same side a shortening by 3 mm. compared with the non-treated control side (88 mm. and 91 mm. respectively). The degree of retardation of growth was in direct proportion to the dosage of radiation applied. There was a marked difference in the sensitivity of the epiphysial cartilage of different bones in the same animal. The distal end of the femur appeared to be far more sensitive than the proximal end of the tibia, in spite of the fact that both are the growing ends of the two bones concerned.

These results suggest that the radium method could easily be modified so as to produce a complete arrest of bone growth without deformity. In that case the whole epiphysis line would have to be equally exposed to radiation. It was shown by histological examination that the enchondral ossification comes to a complete standstill if the necessary dose of radiation is applied. It may be of advantage to combine the traumatizing effect of pegging with the damaging effect of radium by inserting radium needles deep into the epiphysis line. No fear need be entertained that the radium may have an ill effect on tissues other than the epiphysial cartilage, since, according to the law of Bergonié and Tribondeau, tissues with the greatest productive activity are the most susceptible to gamma radiation. Thus gamma rays have an elective effect on the epiphysial cartilage of growing bones.

The radium method has the advantage over other methods that with experience an exact control of bone damage can be achieved by varying the time of exposure and quantity of radium. It should be easy to establish the radium dosage necessary to destroy the germinating power of an epiphysial cartilage, just as it is possible to calculate the erythema dose of the skin. The dosage employed in my experiments may be an indication of the dosage required in human bones, but could not be accepted without further comparative study. Radiologists may find that deep *x* rays will be more practicable for arresting bone growth than radium. It is known that when bone tumours or tuberculosis in juveniles were treated by *x* rays an arrest of bone growth was inadvertently produced. It is up to the radiotherapists to take their choice and work out the details of either of these methods. My present purpose is only to propose practical application of an idea the foundations of which were laid in my earlier experiments.—I am, etc.,

Hong Kong. D. ENGEL.

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Home Nursing and First-aid Lessons for Schoolgirls

SIR,—The raising of the school-leaving age has retained within the education field a final-year group of girls who are maturing mentally as well as physically. This is a time when it is possible to interest them in subjects with a more adult aspect. I suggest that one lesson period a week in the last year of school should be devoted to training in home nursing and first aid. This would provide some 40 sessions of training. This instruction would be an excellent long-term investment for the community. To adopt such a policy nationally would mean that in a few years every shop and office, hotel and café had staff able to give elementary assistance. It would also mean that within a reasonable time every young mother would have a basic knowledge of home nursing which could be of value in the care of her family. A widespread knowledge of home nursing and first aid would relieve pressure on the general practitioner and the district nurse and others and would be to the benefit of all.—I am, etc.,

Brighton. W. S. PARKER.

Treatment of Acute Malaria with Pyrimethamine

SIR,—The paper by Dr. T. Wilson and Dr. J. F. B. Edeson which appears in your issue of January 31 (p. 253) was, I believe, written before Robertson *et al.*[1] had produced from Nairobi conclusive proof that a proguanil-resistant strain of *Plasmodium falciparum* from Malaya was also resistant to pyrimethamine ("daraprim"). It is well known that different "geographical" strains of the malaria parasite vary in their susceptibility to different antimalarial drugs. Nevertheless, it would be a very odd coincidence if there were in the Malaya strains two potential causes for these pyrimethamine "failures"—one, the proguanil cross-resistance proved by Robertson *et al.*, and the other some natural form of resistance unconnected with proguanil-resistance.

It is not without significance that from Assam and Bengal come simultaneous reports of proguanil-resistance (Gilroy[2]) and failures in pyrimethamine treatment (Chakravarty and Chaudhuri[3]). Proguanil has, of course, been widely used for malaria suppression in the tea-gardens of Assam. On the other hand, encouraging results with pyrimethamine are reported from the Delhi area (Jaswant Singh *et al.*[4]) where proguanil-resistance has not been established. Similar reports are being received from various workers in Africa. Wilson and Edeson have rejected cross-resistance as the explanation of their pyrimethamine "failures" because they found that pyrimethamine produced clinical cure in cases which had responded "little or not at all to doses of 300 mg. of proguanil daily for an average of 3.7 days." However, as it appears that the two drugs were given one on the heels of the other, the possibility that the "cure" might be attributable to combined and/or cumulative action cannot be lightly dismissed.

It might not be out of place to emphasize two points which have a bearing on these results. First, the slow therapeutic action of pyrimethamine, which is seen in certain cases and which is mentioned by Wilson and Edeson, is the unavoidable outcome of its mode of action on the malaria parasite, which is effected only at the point of nuclear division. In cases where the synchronization of parasite division has become established, a dose of pyrimethamine given at the right time may have a rapid action. But in primary cases where there is no synchronization, or in cases where the dose is given just after schizogony, a protracted defervescence is inevitable. For this reason, pyrimethamine, though none the less effective in producing an ultimate cure, has certain practical limitations as a therapeutic agent. Second, the risk of the development of pyrimethamine-resistance is remote. While the controlled administration of very small doses of pyrimethamine will undoubtedly produce resistance similar to that caused by irregular proguanil suppression, Coatney, in recent work reported to the American Society of Tropical Medicine and Hygiene at its Annual Meeting in November, 1952, has shown that under experimental conditions resistance cannot be produced by large doses such as those recommended for suppression. If Coatney's observation is confirmed when the drug is in everyday use, this property will add greatly to its usefulness as a suppressant. Reports which are now being received from different parts of the world pay enthusiastic tribute to its efficacy in this role.—I am, etc.,

London, N.W.1. J. S. K. BOYD.

REFERENCES

[1] *British Medical Journal*, 1952, 2, 1255.
[2] *Ann. trop. Med. Parasit.*, 1952, 46, 121.
[3] *J. Indian med. Ass.*, 1953, 22, 155.
[4] In the press.

Sporting Noses

SIR,—Apropos Dr. H. Crichton Miller's letter "Is Boxing Safe for Schoolboys?" (November 15, 1952, p. 1101), I was talking to a man who had a bent nose, and whose father and another son had a similar condition. "Hereditary?" I queried. "Rugger!" was his proud reply.—I am, etc.,

Birmingham. A. P. BERTWISTLE.

"The Slandered Fragrant Weed"

SIR,—No one who has read the article in your issue of December 13, 1952 (p. 1271), on the aetiology of carcinoma of the lung by Dr. Richard Doll and Professor A. Bradford Hill can fail to be deeply impressed by the magnitude of this painstaking investigation. But in a matter of this kind where there is a responsibility for advising the public correctly on the risks of smoking, where they exist, it is essential that no hasty or false conclusions should be drawn from a mass of statistics, for it is a truism that statistics can be made to prove anything. May I therefore emphasize the following points for the benefit of your recent correspondents who suggest that smoking should be incontinently (if not legally) suppressed?

To quote Dr. Doll and Professor Bradford Hill, "We concluded [in our preliminary report] that there is a real association between carcinoma of the lung and smoking, *but pointed out that this is not necessarily to say that smoking causes carcinoma of the lung*" (my italics). The fact that *non-smokers* contract the disease—women 37%, albeit men only 0.5%—to my mind, despite the low incidence in men of non-smokers, proves conclusively that smoking can at most be an *aggravating* factor only and certainly is not the fundamental or basic cause of bronchial carcinomas. The ratio of females to males in the general population, I am told, is six to five. Surely this should give the abolitionist cause to pause and think again before advocating an anti-smoking campaign on the part of our profession. I can think of no shorter cut to unpopularity with all classes of workers than such a campaign based, as it would be, on insufficient data.

The most valuable aspect of this admirable investigation appears to have been completely overlooked, which is odd. Whereas, in certain areas of population, the writers collected some 1,357 lung-carcinoma cases in males, they could collect only 108 cases in females. Yet they show that at least 41% of females in the general population are smokers. The conclusion I draw from this is that the female has a large measure of protection against lung carcinoma which is not shared by the male, and, in view of the fact that differences in occupational conditions by no means explain this discrepancy, one may not unreasonably conjecture that sex-hormone secretion may very likely play a part in determining the low incidence of female cases.

Current literature does not seem to record any clinical trials on these lines—e.g., of stilboestrol (I write subject to correction)—in lung carcinoma. This should be worth extended trial. What is also required is the aid of the biochemist in order accurately to assay the sex hormones in all cases of bronchial carcinoma available to him, with controls, in order to ascertain whether cases in either sex show hormonal abnormalities. This may not be easy, but should not be an insuperable task.

Finally, I quote from a small volume of poetry and prose by Patterson Webb (1925) entitled *The Fragrant Weed*: "Take the case of Hobbes, of Chatworth, who smoked twelve pipes a day—he did not 'shuffle off this mortal coil' until he had seen 92 summers. Likewise Izaak Walton, another devoted lover of the weed, lived to the age of 90. But these youthful smokers have to yield the palm to other renowned veterans like Abraham Favrot, a Swiss, who died in 1769 at the age of 104; or like Jane Garbutt, of Wellbury, Yorkshire, who filled her last pipe in 1856 at the age of 110; or like Heinrich Herz, of Silesia, who continued taking tobacco until he reached the tender age of 142. . . ." All pipe smokers, incidentally.

It is surely obvious that smoking, *per se*, is not the basic cause of bronchial carcinoma but only an accessory after the fact of a probable sex-hormone abnormality in distribution, and that the latter will be found to be the fundamental cause. Moreover, the profession would be ill-advised to sponsor any campaign for the suppression of smoking at this stage of incomplete knowledge. The familiar figure of the greatest of all Englishmen with his famous cigar is still, thank God, with us to engender a remembrance that *mens sana in corpore sano* still holds good.—I am, etc.,

Eastbourne. A. GEOFFREY SHERA.

POINTS FROM LETTERS

Smoking and Cancer of the Lung

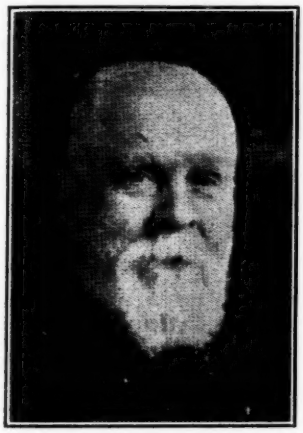
Dr. E. GALLOP (London, S.W.1) writes: In their article on the aetiology of carcinoma of the lung Dr. R. Doll and Professor A. Bradford Hill (December 13, 1952, p. 1271) do not claim that smoking causes cancer of the lung, but only equivocally conclude "that the association between smoking and carcinoma of the lung is real." Two matters should be considered. First, no carcinogen has been found in tobacco smoke, although its presence and ultimate recognition are implied. Secondly, no explanation is given of the fact that there has been no corresponding increase in cancer of the mouth, tongue, pharynx, larynx, nasopharynx, or inside of the nose, although all these areas are exposed to varying amounts of tobacco smoke. The only hint I could get from the article is that the size of the particle of (hypothetical) carcinogen might account for this.

Obituary

E. CLIFFORD BEALE, M.B., F.R.C.P.

We record with regret the death on January 31 of Dr. E. Clifford Beale at the age of 101. He was the oldest member of the British Medical Association.

Edward Clifford Beale was born in Birmingham on October 16, 1851, the son of Mr. W. J. Beale, a solicitor in Edgbaston. The late Mr. Charles Gabriel Beale, one-time Lord Mayor of Birmingham, and the late Sir William Beale, M.P. for South Ayrshire, were his brothers. He was educated at Harrow and at Caius College, Cambridge, where he took his B.A. degree in 1873. He went on to Guy's Hospital, where he qualified in 1878, graduating M.B. in the following year. After holding a number of posts at Guy's he went abroad to continue his studies at Continental clinics. His first staff appointment was as assistant physician to the Great Northern Central Hospital (now the Royal Northern Hospital) in 1881, the year in which he took the M.R.C.P. Six years later he was appointed assistant physician at the City of London Hospital for Diseases of the Chest. In due course he became full physician at both, and he had been consulting physician to both for about the past 45 years.



Dr. Beale was elected F.R.C.P. in 1890, and had been a Fellow for a greater number of years than any other living person. With Sir Clifford Allbutt he revised the section of diseases of the circulatory system in the fourth edition of *Nomenclature of Disease*, published by the Royal College of Physicians in 1906. His specialty was diseases of the lungs, and he published a number of papers on this subject. A keen advocate of the open-air treatment of tuberculosis, he was co-author in 1895 of a textbook entitled *The Treatment of Pulmonary Consumption: A Practical Manual.* He was an original member of the Laryngological Society, and its honorary treasurer from 1899 to 1901.

Dr. Beale had many interests outside his profession, but increasing deafness and failing sight limited his activities during the last years of his life. Even so he was able to go out in a bath-chair quite regularly until the beginning of this winter. He had been a member of the B.M.A. for seventy years when he passed his hundredth birthday, and in a dictated letter to the Editor he expressed his great appreciation of the tribute paid to him in this *Journal* on that occasion.

E. R. GARNETT PASSE, F.R.C.S., F.A.C.S., D.L.O.

We are indebted to Dr. Leighton F. Johnson, professor of otolaryngology in the Boston University School of Medicine, for the following appreciation of Mr. E. R. Garnett Passe (see *Journal*, August 16, 1952, p. 396):

I deem it a distinct honour to present this tribute to my distinguished British colleague Mr. E. R. Garnett Passe. As one who for several years has had an avid interest in autonomic dysfunction as a cause for neurovascular labyrinthian lesions—and having employed the various drugs, orally, intramuscularly, and intravenously, with the usual percentage of successes and failures—I had decided to make a direct attack on the sympathetic surgically when the pioneer work of Mr. Passe presented itself. After considerable correspondence with Mr. Passe, I accepted his kind invitation to come to London in August, 1951, and spend a week with him in his laboratory, in the operating-room, in his office, and in his home. I should like to present very briefly my evaluation of him as a personality, as an investigator, and as a surgeon.

As a personality: He was a very quiet, modest, and kindly person with a keen sense of humour, and he was a delightful companion. His gentle spirit, however, was amply fortified with the courage of his positive convictions. He apparently excelled at everything he did; he was recognized as an expert golfer, horseman, skier, and was a sculptor of ability. As a host he possessed a quiet charm and grace that assured his guests of a delightful evening.

As an investigator: When I visited him in the laboratory, Dr. J. C. Seymour was associated with him, and they were engaged in experiments with the sympathetic in relation to cochlear microphonic potentials. Their approach to the problem, their physiological and anatomical background to this most complex and controversial problem, was very impressive. No exaggerated claims were offered concerning their work. They were quick to give credit to other observers, and Mr. Passe volunteered the prophecy that probably, some time, these same results could be duplicated with drugs. I left the laboratory with the feeling that here was an avid, tireless worker in search of the truth.

As a surgeon: It has been my privilege to see many of the distinguished surgeons of America and Europe operate. I saw Mr. Passe perform a wide variety of surgical procedures, ranging from a dorsal sympathectomy to the fenestration operation. He was a very easy, relaxed, and rapid yet punctilious operator. His surgery was beautiful to observe and performed with consummate skill. It was my opinion that in any group of the world's distinguished surgeons he would rank in the front row.

Mr. Passe was invited to address the New England Otolaryngological Society at its meeting in Boston on November 19, 1952. He kindly accepted this invitation, and shortly after arrangements were concluded we were shocked to hear of his sudden passing. It was then decided to invite Mrs. Passe to present her husband's paper. She graciously accepted our invitation, and with extraordinary courage flew the Atlantic and gave a remarkably successful presentation with inimitable charm. The subject of Mr. Passe's paper was "Surgery of the Sympathetic for Ménière's Disease, Tinnitus Aurium, and Nerve Deafness." The paper was discussed by Dr. Reginald Smithwick, professor of surgery, Boston University School of Medicine; Dr. Derek Denny-Brown, professor of neurology, Harvard Medical School; Dr. George Whitelaw, associate professor of surgery, Boston University School of Medicine; and Dr. M. Stuart Strong, instructor of otolaryngology, Boston University School of Medicine. The concluding remarks by the president of the Society gave assurance to Mrs. Passe that the laboratory and clinical investigations as pioneered by Mr. Passe would go forward in this country, and that the otological department, in co-operation with the Smithwick Foundation of the Boston University Medical School, and the Massachusetts Memorial Hospital were performing these operations with encouraging results.

Surgeon Captain M. H. KNAPP died at Godalming on October 13, 1952, at the age of 84. True to the highest traditions of the Senior Service, he was actively engaged in the welfare of the men in the sick berth branch of the Royal Navy to a month before his death. Born on December 24, 1867, Montague Henry Knapp was the son of

Lieutenant-Colonel C. B. Knapp, and was educated at Queen's College, Cork, and at St. Mary's Hospital, London, qualifying M.R.C.S., L.R.C.P. in 1892, in which year he took also the L.S.A. In the course of his many years of service in the Royal Navy, Surgeon Captain Knapp was medical officer to the training-ships *Lion* and *St. Vincent*, and senior medical officer to the Royal Naval Hospital School at Greenwich and at Admiralty recruiting headquarters. At one time he was honorary director of the naval medical section of the Imperial War Museum and chairman of the Lord Chancellor's Pensions Appeal Tribunal. The work which appealed to him most in his retirement was that concerned with the central council of the Royal Naval Sick Berth Staff Associations, which he founded and of which he was chairman, and we are indebted to Surgeon Commander J. F. HEGGIE, R.N.V.R. (Retd.), honorary secretary of the central council, for the following appreciation : It was through the energy, foresight, and influence of Surgeon Captain Knapp that a central council of distinguished naval medical officers was formed in 1933 as an advisory council to the associations of R.N. sick berth staff (previously benevolent societies) of the three large naval ports, Portsmouth, Devonport, and Chatham. Through the work of this council proper recognition and employment as trained and experienced male nurses came to be assured to the men on retirement to civil life after 12 or 20 years' service in the Royal Navy. During the last war Surgeon Captain Knapp was not idle, especially in regard to the new Nurses Act. He persevered in putting the views of the central council before committees concerned with nursing questions, such as the Athlone and Horder committees, as well as before the Ministries of Health and Labour, the General Nursing Council, and the Royal College of Nursing, and thus the special position and qualifications of the men of the R.N. sick berth branch were made widely known. The help of Admiral Lord Keyes and other interested naval and medical members of the Houses of Parliament was enlisted to support the claims of the sick berth staff, with the result that the Nurses Act of 1943 again reopened the list—closed in 1925—to those then qualified to register as State-registered nurses. The new Act also laid down that sick berth ratings with certain qualifications were to be recognized and named "Service-trained male nurses," and could call themselves nurses and practise as such, although not registered as S.R.N. The reopening of the list to naval personnel was the fulfilment of a suggestion made originally in 1939 by the central council to the Ministry of Health. Unfortunately, owing to the fact that the matter was not sufficiently made known, many men on the active and retired lists, and mostly serving abroad, failed to register before the list was again closed in 1945. It was Surgeon Captain Knapp's contention that men of the sick berth staff who by training, service, experience, and examination had attained the rank of sick berth petty officer should automatically qualify for admission to the *State Register of Nurses*. He long regretted having been unable to ensure this deserved right for petty officers of the sick berth branch, and felt strongly about the want of timely senior official support, about the agreement with the other Services, and about the acceptance of the lower level of Service-trained male nurses for fully and partly trained naval personnel alike. Nevertheless, what was achieved gave him some gratification. There must be many men who, as a result of service during the recent war, became recognized as Service-trained male nurses and with that recognition were enabled to attain registered status the "long way."

By the untimely death of Dr. J. C. C. LANGFORD on January 16 at the age of 55 the medical profession has lost a general practitioner of exceptional qualities. John Charles Cobden Langford studied medicine at Manchester University and St. Bartholomew's Hospital, qualifying M.R.C.S., L.R.C.P. in 1925. After holding appointments at St. Bartholomew's Hospital, the Coventry and Warwickshire Hospital, and the West London Hospital, he settled in general practice at Chiswick in 1926. Always untiring in his attendance upon the sick, to whom he brought the best that science and art had to give, he had in addition a great capacity for encouraging his patients. He possessed an outstanding intellect, and his trained mind enabled him to enjoy wide fields of study. His extensive knowledge of literature, especially of poetry, was often in evidence and added great charm to his conversation. Social occasions with him were times of great delight, and he had a brilliant sense of humour. Early in the last war his house and home were completely destroyed by German bombs, but in spite of that he carried on his work with unremitting courage and without complaint. It is a matter for thankfulness that his final illness was not protracted. To those who knew, loved, and admired him his passing is a very great loss. To his wife, daughter, and two sons we extend our deepest sympathy.—J. L. C.

Dr. H. FOWLER, of Orpington, Kent, died on January 14 at the age of 89. Henry Fowler was born in London on July 20, 1863, and studied medicine at the University of Edinburgh and at the Royal College of Surgeons of Edinburgh, taking the Scottish triple qualification in 1899. Soon after qualifying he went to Siao Kan, in Central China, for the London Missionary Society, and there he planned and supervised the building of a home and hospital for lepers and took charge of the general hospital. In 1921 he became the Far Eastern secretary of the Mission to Lepers, but still remained an honorary missionary of the London Missionary Society. At one time he was president of the China Medical Association. Dr. Fowler returned to England in 1927 and retired from active work in the following year. He was the author of articles on leprosy and on hospital administration in China and was the compiler of a directory of medical missions, which was published in 1930.

Dr. ARTURO CASTIGLIONI, the medical historian and expert on the Renaissance, died in Milan on January 21 at the age of 78. He was born in Trieste on April 10, 1874, and graduated at the University of Vienna in 1896. From 1899 to 1938 he was chief medical officer of the Lloyd Triestino and Italian steamship lines. Castiglioni spent most of his life at Trieste, and there built up his library of more than 20,000 volumes, which was confiscated by the Nazis during the second world war and never recovered. From 1920–38 he was professor of the history of medicine at the University of Padua. Castiglioni went to the United States in 1939 to take up the post of research associate and lecturer on the history of medicine at Yale, where he became professor in 1943. In 1947 he became an American subject, but he returned to live in Italy after retiring from active work. Castiglioni contributed numerous books and papers to the literature of the history of medicine. His *Storia della Medicina*, which appeared in 1927, is similar in plan and scope to Garrison's *History of Medicine*, and contains particularly valuable accounts of the Salerno school and mediaeval and Renaissance Italian medicine. It was later translated into English, French, German, Spanish, and Portuguese, and placed him in the front rank of medical historians. He was an honorary member of the Royal Society of Medicine and of various other learned societies.

A medical practitioner well known in Kensington, Dr. H. E. BARRETT, died in St. Mary's Hospital, London, on January 22 at the age of 75. Henry Edward Barrett was born on March 16, 1877, the son of the late Dr. A. E. Barrett, and received his medical training at St. Mary's Hospital, qualifying M.R.C.S., L.R.C.P. in 1904. He then joined his father in general practice in Kensington, succeeding to the practice on the death of his father in 1916. During the war of 1914–18 he served as a captain in the R.A.M.C. in Salonika and France, and later was assistant medical officer at the Hospital for Officers in Palace Green, Kensington. At one time he was senior clinical assistant

in the throat department of St. Mary's Hospital, and also anaesthetist to the old London Throat Hospital. When war broke out in 1939 he was appointed deputy chairman of a Ministry of Labour and National Service Board at Acton, becoming chairman in 1940 and holding the position until last year. For a short time he was also the chairman of a medical board at the Ministry of Pensions. Dr. Barrett was unfailingly kind and courteous, and after his retirement from practice in 1948 nothing gave him greater pleasure than to meet his old patients, and they were always equally pleased to see him. He leaves a widow and one daughter.

Medical Notes in Parliament

Radioactive Isotopes

Mr. DUNCAN SANDYS, Minister of Supply, made a statement on January 26 on the production of electric power from atomic energy. He said the Government was considering the construction of an experimental atomic power station in which an improved type of natural uranium reactor was enclosed in a pressure shell, the heat produced being transferred by a gas under pressure to a conventional electric power generator. As a by-product this would yield plutonium, which could be used as fuel for further reactors. The Government was also building at Harwell a natural uranium reactor moderated with heavy water, which would produce a much more intense flow of neutrons. This reactor would greatly expand the quantities and variety of radioactive isotopes which could be produced for medical purposes. It would take about four years to complete.

Benefit for Dermatitis

On January 26 Dr. BARNET STROSS asked how many insured workers received in a given year injury benefit on account of dermatitis following irritation by dust or liquids.

Mr. R. H. TURTON replied that in 1950 about 21,000 awards of injury benefit were made for the disease, and about 3,000 initial awards of disablement benefit. At the end of the year there were about 2,200 pensions in payment for the disease, of which 80 were life pensions.

Mobile Radiography Units

Mr. IAIN MACLEOD, on January 26, told Mr. NESS EDWARDS that there were 60 mobile mass radiography units operated by regional hospital boards in England and Wales. The number of staff was 555 at the end of 1951. Approved running expenditure for the financial year 1952–3 was £518,867. Three additional units had recently been allocated and would probably increase the annual cost by £26,000. No major changes in the scale of the service were contemplated.

Control of Antibiotics

In the House of Lords on January 27 LORD ONSLOW, for the Government, introduced the Therapeutic Substances (Prevention of Misuse) Bill. The intention of the Bill is twofold. (1) It would enable additional substances to be brought within the scope of the Penicillin Act, 1947. (2) It would allow the substances covered by the Penicillin Act (as amended) to be sold or supplied, under suitable safeguards, for purposes other than medical. The immediate object of this relaxation is to enable penicillin to be included in the food of livestock where this is recommended as desirable. The Bill proposes that any new substances to be covered should be brought within the scope of the Bill by regulations to be made only after consultation with the Medical Research Council. Similarly, relaxation of any of the safeguards laid down could only be made after consultation with the same Council, and, where appropriate, with the Agricultural Research Council.

The Bill was read a first time.

Dread of Examinations

Mr. MONT FOLLICK, on January 28, spoke on school examinations. He said they spread fear and dread throughout the schools, even ruining the future of the child. He had details of 12 cases, from April, 1948, to the present month, of children committing suicide because they were afraid to face an examination.

Mr. KENNETH PICKTHORNE replied for the Ministry of Education. He said there must be set examinations, and the child was bound to know he was going to have them. Reports ought to be used as much as possible and examinations less. It should not be assumed that examinations were always the reason for a child's suicide or that this was necessarily an argument against examination.

Petition

Mr. LESLIE HALE on January 29 presented a petition signed by 11,416 persons in Oldham and district, calling attention to the loss of the services of a consulting gynaecologist, Mr. A. H. Barber, who had since 1937 been consulting medical officer at Boundary Park Hospital. Mr. Hale said that by the action of the Manchester Regional Hospital Board Mr. Barber had ceased to have the right to give his services under the National Health Service to Oldham. The petition prayed that Mr. Barber be reinstated.

Atmospheric Pollution.—Twenty-seven local authorities have obtained special smoke abatement powers since 1945; two county councils have obtained powers for the use of district councils in their areas. Mr. Macmillan does not consider further general legislation is needed at present.

Surgical Boots.—In England and Wales during the twelve months to May 31, 1952, 48,071 pairs of surgical footwear were issued, costing approximately £400,000. In the seven complete months since then 19,435 pairs have been prescribed.

Deaf Aids.—The estimated cost of batteries supplied to users of Medresco hearings-aids up to December 31, 1951, is £365,000. This excludes administrative and other overheads.

Parrots.—The Minister of Agriculture and Fisheries has made Orders under the Diseases of Animals Act, 1950, which will enable him to deal with diseased parrots. There is no procedure for notifying the police when such a bird is at large.

Medico-Legal

THE SELLY OAK INQUIRY

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

The committee of inquiry set up by the Birmingham Regional Hospital Board to investigate allegations of bad doctoring and bad nursing at Selly Oak Hospital recently concluded a two-day hearing held in public at the Birmingham Council House.[1] The inquiry was made at the request of the Minister of Health as a result of charges made by Professor J. M. Webster, West Midlands Home Office pathologist, at the inquest on Mrs. L. Greaves, who died at the hospital. The Recorder of Birmingham, Mr. Paul Sandlands, Q.C., presided.

Mrs. Greaves was 56 years old and had been completely bedridden for 20 years as a result of a cerebral haemorrhage which had paralysed her right side. Though unable to speak she was able to make herself understood. For the last eight years she had been an inmate of ward M.3 at Selly Oak, and was described by everyone in charge of her as a happy woman in spite of her condition.

It was the practice to lift patients in Mrs. Greaves's condition from their beds and carry them to the bath, for not only did this get them clean more effectively than a bed bath, but it was found to relieve them from their aches and pains. It was also an economical way of using the available nursing

[1] *Birmingham Post*, January 27 and 28.

staff. In ward M.3 there were 55 patients, with a staff consisting only of the ward sister, two assistant nurses, two pupil nurses, and five orderlies.

On October 11, 1952, Mrs. Greaves was taken from bed to have a bath. Afterwards the ward sister was called to her bed, and found her moaning and in distress and pointing to her leg. The sister saw that there was something wrong with her leg, and suspected a fracture. The three nurses who had been lifting her into bed had heard a "crack" as Mrs. Greaves was lifted, although she had not been bumped or jolted in any way.

The house-physician was called and found her shocked and in pain, with her pulse rapid and feeble. He made her as comfortable as he could, and the house-surgeon put her leg into a Thomas splint. She was moved into ward M.1, the surgical ward. Her condition remained very poor, and she had only a fluid diet. She had several bowel motions and showed signs of urinary infection, which the ward sister reported. On October 18 the house-surgeon in the course of examining Mrs. Greaves found a large swelling in the lower part of her abdomen, and noted it in the records, making a provisional diagnosis that it was a tumour of some kind. He did not consider the matter to be urgent, and so did not report it to the consultant surgeon. The priority of treatment established by the consultant surgeon after the accident was to deal first of all with the fracture.

Three days later, on October 21, Mrs. Greaves died.

Professor Webster was asked on behalf of the coroner's officer to carry out a routine necropsy. He found that Mrs. Greaves had had an extensive stroke, that she had had a fracture of the upper third of the femur, that she had a mass of impacted faeces in the lower bowel, which he weighed and found to amount to 2¾ lb. (1.2 kg.), and that she had an ascending infection from the bladder to the kidney.

He came to the conclusion that the fracture was not a spontaneous fracture, although the bone was thin and there was decalcification, because he tried at his examination to snap the bone and could not. He also sawed through it to see how hard it was. He found no bruising or abrasions on Mrs. Greaves's body.

Professor Webster considered that impacted faeces were the cause of the flare-up in the urinary tract. The most obvious cause of the impacting of the faeces would be that she had ceased to have her bowels open either by the fact that she had had no bed-pan or that she had lost the urge by neglecting to listen to the call. He regarded the house-surgeon's failure to report the lump and the consultant's failure to know that it was there until after death as bad doctoring. That constipation to such a degree should be allowed to occur he regarded as bad nursing.

Professor Webster said that he made no allegation of negligence against either the doctors or the nurses.

Dr. Donald Teare, who was called to give evidence on behalf of the doctors in charge of Mrs. Greaves, said that he had studied all the papers in connexion with the death, and had listened to all the evidence given at the inquiry. He accepted the pathological facts found by Professor Webster, but did not draw the same conclusions.

Dr. Teare was satisfied that, taking all the evidence together, the fracture was spontaneous. He would have expected some degree of shock to follow, and infection of the genito-urinary tract was a very common accompaniment. A post-mortem microscopical examination of the kidneys would have indicated the time over which the infection had existed. Constipation was a common occurrence among the chronic sick, particularly when their normal routine was upset. He did not think, from the records and the evidence, that a diagnosis of internal congestion could have been easily made. Treatment to interfere with the constipation could have caused a spread of infection, and there would have been nothing to choose between treating it and leaving it alone. He thought that the house-surgeon's provisional diagnosis of a tumour was an unlikely one.

Dr. Teare said that on Professor Webster's post-mortem findings and with knowledge of the full clinical picture he would not have launched serious allegations of bad doctoring and bad nursing.

After counsel had addressed the Committee on behalf of the nurses and of the doctors in whose care Mrs. Greaves had been, the chairman thanked all who had taken part in the inquiry and said that the report would be submitted to the proper authority in due course.

Universities and Colleges

ROYAL COLLEGE OF PHYSICIANS OF LONDON

At a quarterly comitia of the College held on January 29, with the President, Sir Russell Brain, in the chair, Dr. A. S. Barnes was reappointed the College representative on the Court of Governors of Birmingham University; Dr. D. Hunter and Professor C. A. Keele were appointed members of the Joint Formulary Committee; Sir Weldon Dalrymple-Champneys was appointed delegate to the Health Congress of the Royal Sanitary Institute; and Sir Adolphe Abrahams was appointed the College representative on the Professional Classes Aid Council. It was announced that Dr. D. A. Long had been appointed Milroy Lecturer for 1954.

The following candidates, having satisfied the Censors' Board, were elected Members of the College: E. D. Acheson, B.M., Katharine M. S. Ainley-Walker, B.M., J. F. T. Allison, B.M., T. H. Barrie, M.B., R. N. Beck, M.D., B. Bevan, B.M., Major, R.A.M.C., S. K. Biswas, M.B., Joyce B. Burke, M.D., L. H. Capel, M.B., J. M. Cliff, M.B., Surgeon Lieutenant, R.N., J. D. De Jong, M.D., J. E. Forster, M.B., M. Harington, M.B., E. W. Hughes, M.D., A. F. Knyvett, M.B., R. C. Lewis, M.B., C. J. Lucas, M.B., E. M. McLachlan, M.B., R. J. Marshall, M.D., J. Q. Matthias, M.B., G. W. Scott, M.D., H. M. Sinclair, D.M., W. H. J. Summerskill, B.M., J. L. G. Thomson, M.B., Joan M. Wagner, M.B., M. H. Watson, M.B., J. L. Whitby, M.B., J. C. Woodrow, M.B.

Licences to practise were conferred upon the following 92 candidates who had passed the final examination in medicine, surgery, and midwifery of the Conjoint Board and who have complied with the by-laws of the College: B. L. Anderson, L. P. Balfour-Lynn, R. H. Bartley, Yvonne G. Beeching, Mary A. M. Beeney, F. A. F. Biddle, A. R. Bollen, W. M. S. Boyd, Margaret H. Bradshaw, Joan T. Bruce, Jessie A. S. D. Burns, A. G. N. Calder, R. Y. Calne, H. T. Chadwick, H. W. V. Charlton, N. Crook, Agnes M. S. Curry, Sylvia J. Darke, P. H. Dennison, P. G. Dunbar, W. A. Elkin, Helen R. Ellis, J. E. Evans, J. Ll. Evans, Sheila M. Forbes, R. F. Fouche, N. B. Gillison, H. R. Gompertz, R. M. H. Gompertz, A. H. Gretton, M. C. Guard, Mureen E. Hall, A. G. Harrison, M. D. Heyman, M. D. Hickman, E. C. Howarth, R. J. Hutchinson, Shirley M. Inman, E. M. M. Jackson-Moore, J. A. Jemson, D. C. Jenkins, J. K. Johnson, C. G. Keith, W. J. Lawrence, R. E. Lovelace, K. G. Lupprian, Irene M. McAndrew, R. M. A. McClelland, H. G. McDonald, J. A. McHardy, W. M. McIsaac, E. N. McKenzie, M. C. G. Mantell, J. Marryat, Gillian G. Matthews, L. J. Miller, Margaret E. C. Mitchell, G. L. Money, P. B. Moorhead, K. E. Murray, F. G. M. G. Myer, J. S. Norell, J. J. Parry, N. E. Pitts, M. F. Porter, J. F. Pritchard, D. Ricketts, W. H. Rout, J. A. Rozario, K. E. Schmidt, Rita W. Shannon, C. S. Sheldon, F. G. A. Shenton, G. Singh, J. Stark, I. A. Stewart, B. A. Thompson, R. W. Tooley, A. D. Tuddenham, B. A. Tudgay, J. L. Turk, Maire P. Wallington, J. W. S. Webb, F. L. Whalley, Dorothy J. Whitney, J. R. Williams, A. G. Winfield, D. W. Wood, J. C. Worswick, A. P. J. Wynne-Jones, J. R. Young, K. J. Zilkha.

Diplomas were granted, jointly with the Royal College of Surgeons of England, as follows:

DIPLOMA IN ANAESTHETICS.—I. Jackson, and to the candidates whose names were printed in the report of the meeting of the Royal College of Surgeons of England in the *Journal* of January 24 (p. 226).

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—H. Barakat, M. S. Bopari, M. J. J. T. Becker, T. Mirza.

DIPLOMA IN CHILD HEALTH.—A. Banerjee.

DIPLOMA IN INDUSTRIAL HEALTH.—D. N. Bhatavadekar, W. T. Buckle, P. N. B. Peacock, D. Ramadwar, E. S. O. Smith.

DIPLOMA IN PUBLIC HEALTH.—T. C. R. Archer, E. M. Ensor, S. Jawhar, G. S. Kambourian, A. McGregor, A. K. Mitra, W. T. D. Ray, J. E. C. Robinson, J. P. Scrivener, F. J. Wickremasinghe, O. S. Williams.

Diplomas in Laryngology and Otology, in Pathology, and in Psychological Medicine were also conferred, jointly with the Royal College of Surgeons of England, to the candidates whose names were printed in the report of the meeting of the Royal College of Surgeons of England in the *Journal* of January 24.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

On November 5 the Honorary Fellowship of the College was conferred on Sir Cecil Wakeley and on Sir Reginald Watson-Jones. The Vice-President, Mr. W. Quarry Wood, in presenting Sir Cecil Wakeley, referred to his achievements as surgeon, as author, and as President of the Royal College of Surgeons of England. Mr. R. I. Stirling, in presenting Sir Reginald Watson-Jones, spoke of his career in orthopaedic surgery, culminating in his appointments as Extra Orthopaedic Surgeon to the Queen and as president of the British Orthopaedic Association. Mr. Stirling referred also to the recent conference of the Orthopaedic Surgeons of the English-speaking World, which owed its inspiration and success to Sir Reginald Watson-Jones.

At a meeting of the College held on December 17, 1952, with Professor Walter Mercer, President, in the chair, the following candidates, having passed the requisite examinations, were admitted Fellows: W. A. Anderson, M. I. Anwar, M. Anwer, Agnes U. Campbell, B. M. Corkill, C. M. Couves, R. M. Gaitonde, G. B. Gibson, R. W. L. Heddle, J. H. Hofmeqr, V. M. Kini, I. C. S. Knight, Guan Bee Ong, J. N. Ravalia, J. White.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

At a meeting of the Faculty held on January 5, with Dr. Andrew Allison, President, in the chair, the following were admitted Fellows of Faculty *qua* Physician: Oon Teik Khoo, N. C. Mallik.

CONJOINT BOARD OF IRELAND

The following candidates were duly admitted Licentiates in Medicine and Midwifery on December 5, having passed the final examination in medicine, surgery, and midwifery of the Conjoint Board of Ireland: K. A. Beahan, A. Blake, Mary F. Bonar, R. Calo, G. J. Coghlan, A. W. Eldemire, J. E. Fahy, M. B. Griffin, W. W. Kohler, L. G. Meagher, P. Michalski, J. A. Moffitt, D. MacAlister, F. McCrystal, Marianne Neumann, W. Nolan, Gertrude Shaw, Gustawa Stendig, H. R. Trueman, Audrey Wilkinson.

FACULTY OF RADIOLOGISTS

The following candidates have satisfied the examiners for the Fellowship of the Faculty of Radiologists: *Radiodiagnosis*, P. M. Davies, J. D. Dow, J. R. Dow, E. P. G. H. du Boulay, C. J. Hodson, J. F. K. Hutton, G. M. Sinclair, C. G. Whiteside. *Radiotherapy*, R. Gibb, C. L. Lewis.

ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION

The following candidates were successful at the Association's November examinations for the Diploma in Psychological Medicine: *Part I.*—J. K. Arkle, L. N. Cook, B. W. Davy, R. S. Ferguson, T. E. Hall, T. B. Stephens, R. M. Taylor. *Part II.*—D. S. G. M. Bailey, D. R. Moore, D. G. D. T. Smedberg, W. L. Walker.

Vital Statistics

Industrial Accidents and Diseases in 1952

There were 1,472 deaths from accidents of workpeople in the course of their employment in the United Kingdom during 1952. These comprised 472 in mines and quarries, 804 in factories, docks, etc., and 196 in the railway service. In addition the deaths of 145 seamen were reported.

Cases of industrial disease notified numbered 471, and included 48 of lead-poisoning, 20 of anthrax, 158 of epitheliomatous ulceration, and 217 of chrome ulceration.—*Ministry of Labour Gazette*, January, 1953.

Week Ending January 24

The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,832, whooping-cough 2,792, diphtheria 19, measles 21,882, acute poliomyelitis 24, dysentery 419, paratyphoid fever 8, and typhoid fever 3.

The December Fog

The fog that covered London in the first half of December was determined by absence of wind combined with low temperature. At ground level and for many feet above there was no air movement; smoke, sulphur oxides, and other contaminants therefore increased to concentrations above average. The table below shows how, during the first fortnight of December, the smoke and sulphur dioxide contents of the air increased and then declined. The figures for December 7–8 are the highest recorded at County Hall.

Date	Smoke	Sulphur Dioxide
Dec. 1	0·30	0·090
,, 2	0·49	0·155
,, 3	0·61	0·220
,, 4	0·49	0·144
,, 5	2·64	0·751
,, 6	3·45	0·855
,, 7	4·46	1·339
,, 8	4·46	1·339
,, 9	1·22	0·472
,, 10	1·22	0·472
,, 11	0·32	0·224
,, 12	0·29	0·225
,, 13	0·50	0·263
,, 14	0·32	0·155

NOTE.—Smoke expressed as milligrams of black suspended matter per cubic metre of air. Sulphur dioxide expressed as parts per million by volume.

The above information is taken from a report of the Medical Officer of Health to London County Council, Dr. J. A. Scott, to the health committee of the Council.

Infectious Diseases

The largest changes in the number of notifications of infectious diseases in England and Wales during the week ending January 17 were a decrease of 3,355 for measles, from 24,738 to 21,383; and increases of 351 for scarlet fever, from 1,238 to 1,589; 100 for whooping-cough, from 2,060 to 2,160; and 98 for dysentery, from 214 to 312.

The largest falls in the number of notifications of measles were 638 in Essex, from 2,448 to 1,810; 373 in Warwickshire, from 1,543 to 1,170; 286 in Kent, from 1,397 to 1,111; 257 in Lancashire, from 2,021 to 1,764; and 216 in Hertfordshire, from 700 to 484. The only large exception to the general decline in the incidence of measles was a rise of 91 in Southampton County, where the notifications rose from 1,676 to 1,767. Small rises in the incidence of scarlet fever occurred in most areas, but the only increase of any size was 78 in Lancashire, where the notifications rose from 197 to 275. The largest rise in the number of notifications of whooping-cough was 56 in Lancashire, from 427 to 483, and the largest fall was 30 in Yorkshire West Riding, from 224 to 194.

12 cases of diphtheria were notified, 10 fewer than in the preceding week. This is the smallest number of cases of diphtheria ever notified, being 3 below the preceding lowest level recorded 16 weeks ago. 5 of the 12 cases were notified in Lancashire.

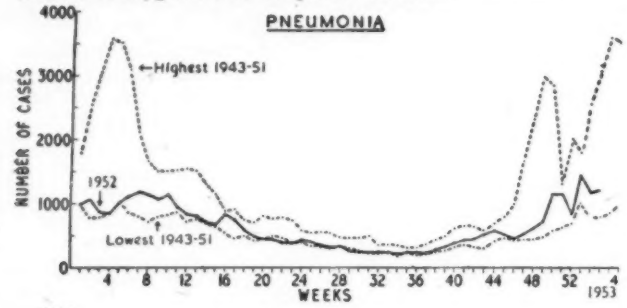
There were 31 cases of acute poliomyelitis—2 more for paralytic and 5 fewer for non-paralytic cases than in the preceding week. The largest returns were Sussex 4 (Midhurst R.D. 2) and Yorkshire West Riding 4.

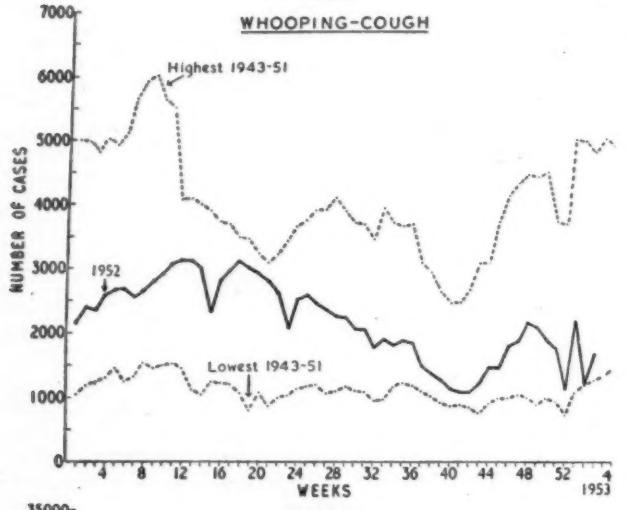
Two new outbreaks of dysentery were reported during the week—41 cases in East Ham C.B. and 10 cases in Yorkshire East Riding, Haltemprice U.D. The other large returns were Lancashire 81 (Preston R.D. 34, Liverpool C.B. 23), Lincolnshire 58 (Grimsby C.B. 57), London 19, and Middlesex 14. The outbreak in Grimsby C.B. has persisted for 18 weeks, and 348 cases have been notified so far.

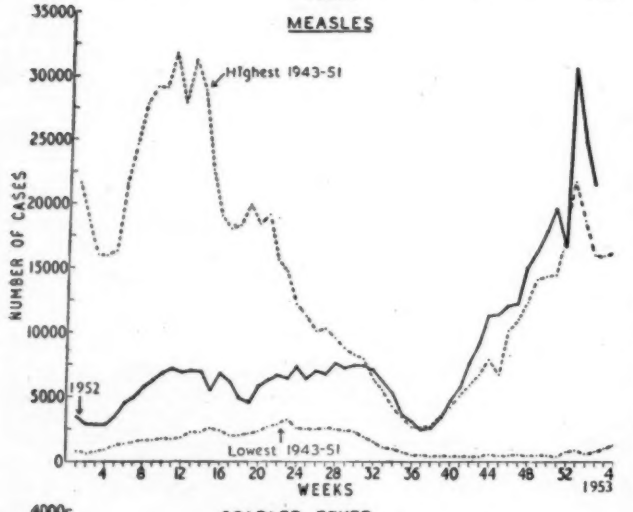
72 deaths were attributed to influenza in the great towns during the week.

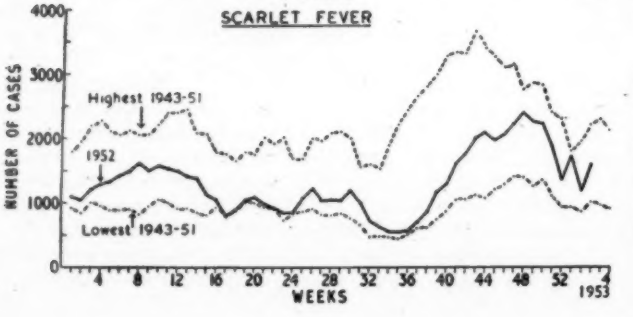
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1943–51 are shown thus - - - - - - - -, the figures for 1952–3 thus ————. Except for the curves showing notifications in 1952–3, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **January 17** (No. 2) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	12	1	9	0	2	33	3	11	0	0
Dysentery	312	19	96		3	315	32	80	6	
Encephalitis, acute	8	1	0	0		3	1	2	0	1
Enteric fever: Typhoid	1	0	0	0	1	3	0	1	1	3
Enteric fever: Paratyphoid	8	1	1 (B)	0	0	3	0	1 (B)	1	
Food-poisoning	46	0		3		134	4		0	
Infective enteritis or diarrhoea under 2 years				11	16				13	16
Measles*	21,383	1777	319	46	114	2,840	33	311	96	57
Meningococcal infection	45	5	30		2	51	4	11	0	2
Ophthalmia neonatorum	40	2	15	1		34	8	7	0	2
Pneumonia†	1,204	66	333	32		1,056	67	304	1	2
Poliomyelitis, acute: Paralytic	25	0	3	1	5	33	4	4	0	
Poliomyelitis, acute: Non-paralytic	6	0				3	2			
Puerperal fever§	212	24	15	3	1	247	35	6	3	
Scarlet fever	1,589	65	332	44	55	1,055	68	248	32	37
Tuberculosis: Respiratory			128	26				114	27	
Tuberculosis: Non-respiratory			30	6				23	5	
Whooping-cough	2,160	99	192	53	80	2,394	88	391	84	54

DEATHS In Great Towns	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	0	0	0	0	0	1	1		0	0
Dysentery	0	0		0		1	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0		0	
Infective enteritis or diarrhoea under 2 years	13	3	2	0	1	20		0	0	1
Influenza	72	14	2	1	0	31	6		1	0
Measles		0	0	0	0		0		0	0
Meningococcal infection		1	1				1			
Pneumonia	491	87	36	14	11	350	50		13	15
Poliomyelitis, acute	2	0			0	3	1			0
Scarlet fever		0	0	0	0		0		0	0
Tuberculosis: Respiratory	182	32	17	4	12	150	15	29	3	11
Tuberculosis: Non-respiratory		1	3	0	0		3	2	0	3
Whooping-cough	0	0	0	0	1	3	0		0	1
Deaths 0–1 year	293	34	41	9	14	326	43	50	11	25
Deaths (excluding stillbirths)	7,697	1300	773	149	207	6,408	958	779	140	199
LIVE BIRTHS	7,548	1113	965	264	419	7,644	1099	975	211	439
STILLBIRTHS	180	24	25			218	21	24		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Director-General of W.H.O. Nominated.—The Executive Board of the World Health Organization has nominated Dr. Marcolino Gomez Candau (Brazil) to succeed Dr. Brock Chisholm as Director-General. Dr. Chisholm is due to retire in July after five years in office, and under the constitution of W.H.O. his successor must be appointed by the World Health Assembly on a single nomination by the Executive Board. Born in 1911, Dr. Candau received his medical education at Rio de Janeiro and at the Johns Hopkins University, Baltimore. After holding numerous public health appointments in Brazil culminating in that of superintendent of the Serviço de Saúde Pública (a co-operative public health organization of the Brazilian Government and the Institute of Inter-American Affairs), Dr. Candau joined the staff of W.H.O. in 1950 and served at its headquarters in Geneva, first as Director of the Division of Organization of Public Health Services and later as Assistant Director-General in charge of the Department of Advisory Services. In December, 1951, Dr. Candau left W.H.O. headquarters on being appointed Assistant Director of the Pan-American Sanitary Bureau.

W.H.O.'s Financial Troubles.—As a result of a review by the United Nations Technical Assistance Board of the present programme of help to underdeveloped areas, lower priority has been recommended for many health projects. W.H.O. is now faced with the threat that its technical assistance funds for this year may be cut to $5m., although its present commitments already amount to nearly double that amount. Not only is W.H.O. affected directly, but countries collaborating in the health projects have set aside large sums towards them, estimated at $40m. for this year. According to the executive chairman of the Technical Assistance Board, who went to Geneva last month to explain matters to the W.H.O. Board, the financial position may not prove as bad as appears at present. Apparently a large part of the trouble is because many Governments supporting the technical assistance scheme have not yet fulfilled their pledges of assistance for 1952. This, he said, accounted for the cuts. The real state of affairs would become clear at a Technical Assistance Conference in New York this month.

Student Health Services.—In a progress report, adopted at last week's comitia of the Royal College of Physicians of London, the College's social and preventive medicine committee reviews the present state of student health services in England and Wales. On the whole students in the provinces are well provided for, though more could be done by some universities in the way of inspecting lodgings. Oxford, where a proposal to establish a student health service was recently turned down, is named in the report as being exceptional in lacking a comprehensive service of the kind recommended by the committee (see *British Medical Journal*, 1946, **1**, 280). In London there is great variation: medical students suffer no neglect, but the plight of the non-medical students is regarded as much less satisfactory than in the provinces. With two notable exceptions (University College and Imperial College), the non-residential colleges in London, with a student population of more than 6,000, have little in the way of student health facilities. Of them it is said, "Interest in the preventive aspect of student health is confined to mass radiography, and the college authorities seem to regard this as all that is incumbent on them to do." These authorities are invited by the committee to reconsider their responsibilities.

Medical Team to Visit India.—Three Britons are included in a distinguished international team of 15 medical scientists which has just left for India. They are Sir Alexander Fleming, Mr. H. Osmond-Clarke, and Professor R. R. Macintosh. The team is sponsored jointly by W.H.O. and the Unitarian Service Committee of Boston, U.S.A. The members of the team are to work for two months side by side with Indian scientists at the Universities of Bombay and Madras. Some of the members of the team will go on afterwards to Indonesia. Specialties represented include physiology, microbiology, pharmacology, child health, surgery, anaesthetics, radiology, and public health administration.

Hecogenin for Cortisone.—In the Medical Research Council's last annual report (see *British Medical Journal*, July 26, 1952, p. 211) mention was made of hecogenin as a promising starting-point for a synthesis of cortisone. Hecogenin was known as a rather scarce constituent of certain species of Central American yam, but M.R.C. workers reported its discovery in high concentration in sisal juice, a plentiful waste product of the sisal industry. It is now learnt that the National Research Development Corporation is sponsoring a pilot plant in East Africa for a detailed study of the methods of extracting and processing the juice. Scientific direction is provided by a laboratory unit under the joint auspices of the M.R.C. and the East African Industrial Research Board.

Failure of a Grafted Kidney.—Marius Renard, the young Frenchman on whom a kidney-grafting operation was performed in Paris just before Christmas, died on January 27. His kidney was damaged in an accident, and only after nephrectomy had been performed was it realized that it was his only one. Renard's mother gave one of her own kidneys for grafting in an attempt to save her son's life. The theoretical aspects of kidney-grafting are discussed in a report elsewhere in this issue (p. 329).

American Doctors in Britain.—The Horse Shoe Club, which was formed in 1932 with the purpose of fostering friendship and the exchange of medical research and clinical workers between the United States and Britain, is appealing for information about American doctors temporarily resident in this country. It is intended to compile a list of their addresses. The Club, whose chairman is Dr. Geoffrey Bourne, maintains an address list of its own members indicating their specialist medical interests for the benefit of visiting American doctors. Membership is open to doctors who have studied in America or who grant facilities for Americans to work in their departments, and to interested laymen. Information about visiting Americans, or inquiries about membership, should be addressed to the honorary secretary, Dr. Claude Nicol, St. Bartholomew's Hospital, London, E.C.1.

Bequests from the Laity.—Miss Lydia Crossley, of Harrogate, bequeathed approximately £31,000 (the residue of her estate) equally to Harrogate and District General Hospital, the Yorkshire Home for Chronic and Incurable Cases, Harrogate, and the Royal Baths Hospital and Rawson Home for Incurables, Harrogate. Miss Margaret Frazer Dallas, of Plymouth, who left estate valued at £28,000, bequeathed the residue, after several small legacies, equally to the Marie Curie Hospital, Hampstead, the British Empire Cancer Campaign, the Royal U.K. Beneficent Association, and St. Dunstan's.

Professor Robert Platt has been invited by the medical students of Witwatersrand University to be their "visiting lecturer" for two months. He began his lectureship this week and will be back in this country in April.

Dr. F. M. R. Walshe, F.R.S., consulting physician to University College Hospital, is to deliver this year's Ferrier Lecture before the Royal Society. The lecture was founded in 1928 in memory of Sir David Ferrier, and is on a subject related to the advancement of natural knowledge on the structure and function of the nervous system.

Dr. H. D. Chalke, a divisional medical officer of the London County Council, and **Dr. E. R. Hargreaves,** deputy medical officer of health, Cornwall, divide the one hundred guineas prize offered by the National Association for the Prevention of Tuberculosis for an essay by a public health medical officer on "Modern Measures for the Control of Tuberculosis, as practised by Local Health Authorities in Great Britain."

Sir Heneage Ogilvie's appointment as praelector in the faculty of medicine at St. Andrews University (see *Journal*, January 17, p. 169) is for one week only. Immediately afterwards he will be returning to London.

Emergency Bed Service: Applications and Admissions.—During the seven days ending February 2 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 2,065, of whom 88.47% were admitted. In spite of this higher level of acceptances, on February 2 the previous red warning was changed only to yellow. This is because the present favourable trend could easily be reversed at very short notice.

COMING EVENTS

Education in Nutrition.—The Nutrition Society is holding a whole-day symposium at King's College of Household and Social Science, Campden Hill Road, London, W.8, on Saturday, March 7, on the subject of "Education in Nutrition in the United Kingdom." The chairman will be Professor J. Yudkin. Further particulars may be obtained from the programmes secretary, Dr. R. J. L. Allen, Monkhouse and Glasscock Ltd., Snow's Fields, London, S.E.1.

Course on Rheumatic Diseases.—A week-end course on "The Chronic Rheumatic Diseases" is to be held at the Rheumatism Unit of St. Stephen's Hospital, Chelsea, on March 21 and 22. The course will be opened by Dr. P. M. F. Bishop, and will include lectures and practical demonstrations. Further details may be obtained from the secretary, Fellowship of Postgraduate Medicine, 1, Wimpole Street, London, W.1.

NEW ISSUES

British Journal of Neurology, Neurosurgery and Psychiatry.—The next issue (Vol. 16, No. 1) will be available in a week's time. The contents include:

APHASIA. Sir Charles Symonds.
THE EFFECTS OF METHEDRINE AND OF LYSERGIC ACID DIETHYLAMIDE ON MENTAL PROCESSES AND ON THE BLOOD ADRENALINE LEVEL. D. W. Liddell and H. Weil-Malherbe.
INVESTIGATION OF AMNESIC DEFECTS BY PROGRESSIVE PROMPTING. Moyra Williams.
THE STUDY OF THE PARAESTHESIAE INDUCED BY COLD. John Marshall.
AFFECTIVE EPILEPSY. L. van der Horst.
THE EPILEPTIC THRESHOLD IN SCHIZOPHRENIA. J. Hoenig and D. M. Leiberman.
DISTURBANCES OF OCULOMOTOR FUNCTION ACCOMPANYING EXTRADURAL HAEMORRHAGE. S. Sunderland and K. C. Bradley.
THE INTRA-ARTERIAL INJECTION OF NEOSTIGMINE AS A DIAGNOSTIC TEST IN MYASTHENIA GRAVIS. E. C. Hutchinson and W. B. Matthews.
THE NEUROLOGICAL ASPECTS OF DERMATOMYOSITIS. W. B. Matthews and J. C. Burne.

Issued quarterly; annual subscription £2 2s., single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

Details in this column are necessarily brief. Further information and tickets where required (marked ●) should be obtained from the institution concerned.

Monday, February 9

BRITISH SOCIETY FOR THE STUDY OF ORTHODONTICS.—7.30 p.m., Dr. H. R. E. Wallis: Medical Aspects of Mal-occlusion.
INSTITUTE OF NEUROLOGY.—5 p.m., Professor E. Bay (Heidelberg): The So-called Visual Agnosias.
INSTITUTE OF PSYCHIATRY.—5.30 p.m., Dr. E. Stengel: lecture-demonstration for postgraduates.
MEDICAL SOCIETY OF LONDON.—8.30 p.m., discussion to be introduced by Dr. W. E. Snell and Mr. V. C. Thompson: Recent Methods in the Treatment of Pulmonary Tuberculosis.

Tuesday, February 10

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. Honor B. Fell, F.R.S.: Organ Culture in Biological and Medical Research.
CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, 8.30 p.m., discussion to be opened by Mr. J. Betjeman, Sir Heneage Ogilvie, and Mr. Gilbert Harding: The Importance of Leisure.
● INSTITUTE OF DERMATOLOGY.—5.30 p.m., Mr. A. K. Monro: Hypostatic Eczema and Ulceration.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Milroy Lecture by Dr. W. R. S. Doll: Bronchial Carcinoma, Incidence and Aetiology.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor T. E. Cawthorne: Surgery of the Temporal Bone.
WEST END HOSPITAL FOR NERVOUS DISEASES.—5.30 p.m., Mr. G. C. Knight: Treatment of Head Injury.

Wednesday, February 11

● INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Benign Tumours of the Corium.
INSTITUTE OF UROLOGY.—At St. Paul's Hospital, W.C., 4.30 for 5 p.m., Mr. A. R. C. Higham: Enuresis.
LONDON UNIVERSITY.—At London Hospital Medical College, 5 p.m., Professor A. Giroud (Paris): Factors of Abnormal Development.
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Dr. John Burns Lecture by Dr. R. R. Willcox: The Treponemal Diseases.

Thursday, February 12

ALFRED ADLER MEDICAL SOCIETY.—At 11, Chandos Street, W., 8 p.m., Dr. M. N. Pai: Indications for Hypnosis in Psychotherapy.
BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor P. C. C. Garnham: Life Cycle of the Malaria Parasite.
GLASGOW UNIVERSITY MEDICO-CHIRURGICAL SOCIETY.—At Glasgow University Union, 7.30 p.m., Group Captain W. K. Stewart: Aviation Physiology.
● HUNTERIAN SOCIETY.—At Savoy Hotel, W.C., 7 for 7.30 p.m., annual dinner.
● INSTITUTE OF CHILD HEALTH.—5 p.m., Dr. E. M. Creak: Behaviour Problems in Early Childhood.
● INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Mycology—Diagnostic Techniques.
LIVERPOOL MEDICAL INSTITUTION.—8 p.m., Mr. F. R. Edwards: Present Position of the Surgery of the Heart and Great Vessels.
OXFORD UNIVERSITY.—At Nuffield Orthopaedic Centre, 8.30 p.m., Mr. H. J. Seddon: Colonial Medicine.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Dr. R. Lewthwaite: Typhus Group of Fevers (with lantern slides).
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Milroy Lecture by Dr. W. R. S. Doll: Bronchial Carcinoma, Incidence and Aetiology.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor W. Hynes: Results of Pharyngoplasty by Muscle Transplantation in "Failed Cleft-palate" Cases, with Special Reference to the Influence of the Pharynx on Voice Production.
ST. ANDREWS UNIVERSITY.—At Physiology Department, Dundee, 5 p.m., Professor J. W. McLeod, F.R.S.: Nature of Anaerobic Infections and their Control.

Friday, February 13

ASSOCIATION OF INDUSTRIAL MEDICAL OFFICERS (LONDON GROUP).—At London School of Hygiene and Tropical Medicine, 5.30 p.m., clinical meeting.
● INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. H. Gordon: Benign New Growths.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—4 p.m., Hunterian Oration by Mr. L. E. C. Norbury: The Hunterian Era—its Influence on the Art and Science of Surgery.
ROYAL INSTITUTE OF PHILOSOPHY.—At University Hall, 14, Gordon Square, W.C., 5.15 p.m., Professor J. N. Findlay: Wittgenstein's Philosophical Studies.
ROYAL MEDICAL SOCIETY, Edinburgh.—8 p.m., Sir Clement Price Thomas: Carcinoma of the Lung.

Saturday, February 14

SOUTH-EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At London School of Hygiene and Tropical Medicine, 10.30 for 11 a.m., Dr. Neville Oswald: Bronchitis.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Bower.—On January 21, 1953, at the Queen Elizabeth Hospital, Birmingham, to Christine (formerly Aitchison), M.B., D.Obst.R.C.O.G., wife of B. D. Bower, M.B., M.R.C.P., a son.
Davies.—On January 22, 1953, to Dr. Winifred M. Davies (formerly Haigh), wife of Dr. D. M Davies, Meadehurst, Glebelands Road, Prestwich, Lancs, a son.
Maxwell.—On January 25, 1953, at St. Mary's Hospital, London, W., to Joan (formerly Eggleston), wife of Dr. W. Murray I. Maxwell, a son—Christopher Murray.

MARRIAGES

Lovibond—Carew-Jones.—On December 12, 1952, in London, John Locke Lovibond, T.D., M.D., F.R.C.P., to Mary Carew-Jones.

DEATHS

Anderson.—On January 18, 1953, John Anderson, M.B., C.M., of 7, Ashcroft Road, Ipswich, Suffolk, aged 83.
Barrett.—On January 22, 1953, at the Lindo Wing, St. Mary's Hospital, London, W., Henry Edward Barrett, M.R.C.S., L.R.C.P., of 33, Holland Park, London, W., aged 75.
Bellis.—On January 19, 1953, at his home, Wernto, Llanfairfechan, Caern, Thomas Bellis, M.B., Ch.B.
Bisset.—On January 20, 1953, at 37, Bankhurst Road, London, S.E., Mary Ronald Bisset, M.B., Ch.B., late of Bhiwani, India.
Burden.—On January 18, 1953, at Pine Grange, Bournemouth, Hants, Henry Burden, C.I.E., F.R.C.S., Colonel, I.M.S., retired, aged 85.
Clark.—On January 20, 1953, at Peebles, Scotland, Robert Veitch Clark, M.B., Ch.B., D.P.H., formerly of Manchester, aged 76.
Hodges.—On January 17, 1953, at Bulan, Perranporth, Cornwall, Richard Harold Hodges, M.C., L.R.C.P.&S.I. & L.M., Major, R.A.M.C., retired, aged 65.
James.—On January 22, 1953, John Angell James, M.R.C.S., L.R.C.P., of "Dusk," Elmlea Avenue, Bristol, aged 89.
Joy.—On January 20, 1953, at Chichester, Norman Humbert Joy, M.R.C.S., L.R.C.P., late of Bradfield, Berks, aged 78.
Paget-Tomlinson.—On January 20, 1953, at Summerhill, Ulverston, Lancs, Edward Edmondson Paget-Tomlinson, M.D., aged 70.
Stonham.—On January 20, 1953, at his home, Worthing, Sussex, Thomas George Stonham, M.D., aged 95.
Webb.—On January 23, 1953, in a nursing-home, Cambridge, Charles Carew Webb, M.B., B.Ch., D.P.H., of 8, Millington Road, Cambridge, aged 87.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Non-specific Ulcer of the Caecum

Q.—*I understand that recently a condition of ulcer of the caecum has been recognized. I believe the aetiology is unknown and the prognosis good. I am excluding such conditions as tuberculosis, neoplasm, and amoebiasis, together with actinomycosis. Can you please give me any information on this condition?*

A.—Non-specific ulcer of the caecum was described as long ago as 1882. The aetiology is unknown, but the site of these ulcers, above the ileo-caecal valve, is constant and they are liable to all the complications of the ordinary peptic ulcer—that is, perforation, haemorrhage, stenosis, and penetration with local abscess formation. It is usually one of these happenings that leads to their discovery—or the formation of a mass misdiagnosed as a neoplasm. In considering their aetiology and site the caeco-colic region has been likened to a "second stomach." Sufferers from these ulcers are habitually constipated. The most recent reference to them is an article on four cases by Sir David Wilkie in *Surgery* (1937, **1**, 655).

Allergic Rhinitis

Q.—*An elderly lady has suffered for the last two years from allergic rhinitis, and the only relief has been from an antihistamine drug. An allergy specialist has failed to help: cautery and surgical removal of redundant mucosa have given only temporary relief. Teeth have been dealt with. Is there any other treatment which might be worth trying?*

A.—The management of a case of allergic rhinitis may demand all the ingenuity and resources of a team of specialists before the condition can be remedied. At the outset it should be regarded as the local manifestation of a general disturbance, and the patient should be investigated to see if there is sensitivity to any inhalant. This calls for careful history-taking and skin-testing. If there are any particular substances to which the subject is sensitive these should, so far as possible, be eliminated; at the same time a course of desensitizing injections should be given. If the subject is sensitive to many things, a course of injections of mixed inhalants should be considered. Allergic rhinitis sometimes responds to antihistamines, which may even be given for a prolonged period. Examination of the nose may disclose a sharp spur or deflection of the septum acting as a trigger, and relief may follow the straightening of the septum. If the allergic rhinitis seems to be unilateral, cauterization of the inferior turbinals and septum sometimes brings relief. Local treatment could also include a spray composed of one of the synthetic vasoconstrictors with an antihistamine, or in very severe cases a spray composed of a vasoconstrictor combined with 1% cocaine solution might be helpful if used sparingly.

H.P.C. Treatment for Rheumatoid Arthritis

Q.—*What is the H.P.C. treatment for rheumatoid arthritis? Is it useful, and what are the drawbacks?*

A.—H.P.C. (hydroxy-phenylcinchoninic acid) has been tried in chronic arthritis because in the experimental animal it causes a decrease in the ascorbic acid content of the adrenal gland and an increase in uric acid excretion. This suggested it might have an action like A.C.T.H. Clinical trials have been undertaken in a number of centres in America, and on the whole the results in arthritis have been disappointing. In a recent trial in this country in some collagen diseases (*British Medical Journal*, 1951, **1**, 383) the drug was used in rheumatic fever, polyarteritis nodosa, scleroderma, and lupus erythematosus. The recommended dosage is 20 to 40 mg./kg. body weight per day, and it should be given in the course of two hours after the morning meal, the dose being divided into three or more parts to avoid nausea. The toxic manifestations reported have been nausea, anorexia, vomiting, and diarrhoea, with occasionally blood in the stools. This may occur in the first few days and is said to pass off with continued therapy. In addition, dysuria, skin rashes, and fever have been seen with this drug.

Plastics for Thermometers

Q.—*The breakage of clinical thermometers must cost the public many hundreds of pounds every year. Is there any reason why the glass should not be replaced by some plastic material?*

A.—The chief reason why a plastic material would probably not be successful for the manufacture of clinical thermometers is its lack of stability. Clinical thermometers, though cheap and made in large numbers, are instruments of precision. It is essential in any good thermometer that the volume of the bulb should remain constant and free from thermal hysteresia—that is, the volume must return exactly to its previous size after any change of temperature. Clinical thermometers are made of special glass chosen for this property; but plastics, in general, do not possess it, and a thermometer made from them would be very erratic in its readings. Furthermore, it is probable that much development work would be necessary before it would be possible to make capillary tubes as fine and uniform in plastic materials as in glass, or to form in them the short constriction which enables the clinical thermometer to read the "maximum" value of the temperature reached.

Intravenous P.A.S.

Q.—*Is P.A.S. of greater value to the tuberculous patient if given by the intravenous route? In France particularly this method appears to be popular, as it is said to avoid the gastro-intestinal upset when P.A.S. is taken by mouth.*

A.—Considerable claims have been made by Paraf and his co-workers in France in favour of the intravenous administration of P.A.S. They believe it to be considerably more effective than administration by mouth, and claim also that the results are better than those obtained with streptomycin. Gastro-intestinal upset is certainly avoided, but it is difficult to interpret the available evidence claiming superior therapeutic effect.

Phenytoin Sodium and Eclampsia

Q.—*In view of its anticonvulsant properties, is phenytoin sodium of special value in eclampsia?*

A.—The writer is not aware of any published reports on the use of phenytoin sodium in eclampsia. In theory there are certain objections to its use. Although it is an anticonvulsant in epilepsy, it apparently does not control convulsions of all types and origins. This argument may not apply here, however, because there is some evidence that the fits of eclampsia and epilepsy have a similar basis. This is an old view recently elaborated by R. R. Macintosh in *J. Obstet. Gynaec. Brit. Emp.* (1952, **59**, 197). However, even in epilepsy the drug prevents rather than controls fits, so in eclampsia the onset of its action would probably be delayed too long for it to be useful. Parenteral administration, which might be contemplated to ensure a quicker effect, is contraindicated because of the toxicity of the drug; it can cause respiratory embarrassment, which would be a serious matter in eclampsia. Again, any sort of oral administration is usually impossible in established eclampsia.

If phenytoin sodium has any place in the treatment of eclampsia it is perhaps as a prophylactic which could be given orally to women suffering from pre-eclampsia, and especially those threatening to have fits. Even in such cases, however, it might not be so useful as barbiturates, in that it has no sedative action—which is generally thought to be desirable in these cases.

Tropical Diarrhoea

Q.—*On a recent visit to Madeira, an unduly large proportion of visitors were afflicted by an epidemic form of diarrhoea, which was locally known as "Madeira fever." To me the condition suggested a mild bacillary dysentery. Can you please tell me if anything is known of the aetiology of this condition? If it is not a bacillary dysentery, what is it, and what is the best treatment?*

A.—In almost every tropical town or region the locally occurring alimentary upsets are given a special designation. There are, for example, "Gyppy tummy" in Egypt, "Delhi tummy" and "Bombay belly" in India, and in Madeira "Madeira fever." The vast majority of these upsets are due to mild attacks of bacillary dysentery, though some cases of amoebic dysentery and other infections are at first labelled with the local term. There is much to be said for ceasing to use these local terms and encouraging more accurate diagnosis.

Recurrent Parotid Enlargement

Q.—*Is there any known relationship between menstruation and recurrent parotid enlargement? A girl aged 14 suffers from a recurrent enlargement of the right parotid gland. It lasts for about a day only, and occurs regularly each month six days before the onset of the menses. Radiography fails to show any sign of calculus. What treatment is advised?*

A.—The commonest cause of recurrent parotid enlargement is a mild parotitis usually due to infection with *Streptococcus viridans*. Less common causes are strictures of the duct and occasionally allergic conditions. On the other hand, there appears to be no known direct relationship between menstruation and recurrent parotid enlargement, though an indirect relationship is possible.

There are certain factors in connexion with recurrent parotid enlargement which might possibly have a bearing on the present case. The condition is commoner in the female sex; in most cases there is some disturbance of the chewing mechanism; and in some cases there is a mild psychological factor. The disturbance of the chewing mechanism may be an actual dental disease, ill-fitting dentures, etc., or even a habit of bolting food. Just as acute parotitis occurs in patients who are not eating normally and have an altered bacterial flora in the mouth, so recurrent enlargements occur in patients who for one reason or another have some disturbance in the chewing mechanism. Psychological factors may also be of some importance. They do not, however, tend to any degree of severity, but it is certainly true that the recurrent attacks may be related to some mild emotional disturbance.

Treatment is not always easy. Dental faults and any local infection should be dealt with, and obviously chewing habits must be considered. Both bacteriological examination of a catheter specimen of parotid saliva and sialography may be advisable. In the mildest cases the patient should be shown how to empty the gland in a forward direction in the line of the duct for five minutes morning and evening, and this may be enough to relieve the condition. In the more serious conditions it may be necessary to dilate or slit the duct and to follow this up with intermittent dilatations over a few weeks. In the absence of duct obstruction, mild cases, particularly those due to *Str. viridans*, may sometimes be helped by *x*-ray treatment.

Penicillin-resistant Impetigo

Q.—*I have treated about fifteen cases of impetigo recently. All but one or two of the cases failed to respond to penicillin cream (which I have found effective in the past). The penicillin-insensitive cases were quickly cured with chloramphenicol cream. The impetigo seemed to lack the usual yellow crusting, and had the appearance of non-specific sores. Is there any evidence of a spread of impetigo caused by penicillin-insensitive staphylococci or streptococci?*

A.—Impetigo had in recent years become a rare disease in dermatological clinics. But during the past year or so impetigo has been returning to these clinics, sometimes in epidemic form, and the pyogenic organisms have in most instances been insensitive to penicillin.

NOTES AND COMMENTS

Intercourse after Syphilis.—Dr. P. A. CLEMENTS (London) writes: The answer under this heading ("Any Questions?" January 10, p. 115) seems to me to be dangerous. It is well known that a person may remain serologically negative for many more than six months after what eventually proves to have been insufficient treatment. It is incorrect to say that there is no evidence that semen itself contains *S. pallida*. To quote only from an immediately available article, Harrison in Vol. VIII of the Medical Research Council's *System of Bacteriology*, 1931, p. 208, quotes evidence to the contrary by Finger and Landsteiner and by Noeggerath and Staehelin in secondary syphilis (and a relapse after insufficient treatment of early syphilis may well be into the second stage) and in latent syphilis by Kertesz (by inoculation) and Warthin (histologically).

Dr. T. E. OSMOND (Ashford) writes: Is not your expert overlenient in allowing sexual intercourse six months after completion of treatment of syphilis? It is well known that the relapse rate in secondary syphilis treated by modern methods often exceeds 10%. And though most relapses occur within the first six months a not inconsiderable number occur later. Surely spirochaetes are present at times in the semen, but does their presence necessarily indicate syphilitic vesiculitis and vasitis, and, if so, what is the evidence?

OUR EXPERT writes: It should be realized that the articles by Finger and Landsteiner and by Noeggerath and Staehelin appeared in 1906—i.e., four years before Ehrlich introduced "salvarsan"; also that the work of Warthin (1918) and Kertesz (1928) was not confirmed by others. Pariser (1942) was unable to transmit syphilis to susceptible animals by seminal fluid obtained from men with early syphilis unless it had been contaminated with *S. pallida* while passing over an open lesion containing the organism. Stokes and his collaborators (1944) state that "it is not believed at the present time that syphilis can be transmitted to the ovum by semen of an infected male." In his query Dr. Osmond admits that most relapses occur within the first six months. The writer has personally never seen one after that period, and those recorded in the literature, chiefly in the United States, are regarded as reinfections, not relapses. There is much evidence on this in the paper by Pariser.

REFERENCES

Pariser, H. (1942). *J. invest. Derm.*, **5**, 311.
Stokes, J. H., Beerman, H., and Ingraham, N. R. (1944). *Modern Clinical Syphilology*. Philadelphia

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